Angina Pectoris and Myocardial Infarction

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With Special Reference to the Autonomic Nervous System

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To the memory of my son

Frederick Monteser Miller

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Preface

EVEN a cursory survey of the extensive literature on angina pectoris and myocardial infarction renders it apparent that many problems which beset workers and writers in this field are still with us Briefly and in the main these are confusion arising in the concept and use of the terms anginal pain angina pectoris and acute myocardial infarction with or without acute coronary occlusion lack of knowledge of the physiology of pain in general and of anginal pain in particular the comparatively large number of unrevealed or only partially explored pathways for the transmission of anginal pain, almost total ignorance of the genesis and mechanics of emotional elements which belong with the disorders in question and above all failure to appreciate that central and peripheral autonomic reactions underlie the clinical features associated with angina pectoris and acute myocardial infarction and with many acute extracardiac conditions which simulate these disorders

The original volume which appeared in 1939 and its reissue with an appendix three years later dealt with all these problems but paid special attention to two objectives (1) a comprehensive and accurate delineation of the cardiac innervations (2) the concept that the autonomic nervous system functions by a unitary or mass action to produce wide and varied clinical manifestations It was further stressed that these manifestations as well as the mechanism of referred pain are common overlapping features which underlie most acute explosive cardiac as well as noncardiac *episodes*

To help toward the first objective a series of anatomic charts of the cardiac innervation was carefully developed The charts or drawings *were presented* as a progressive eries from the implest to the more complicated each in turn adding a portion of the cardiac nerve supplies Each drawing was designed to carry a concept or anatomic structure absent in the immediately preceding drawing and all were to be studied in the *order of their arrangement* Schematic presentation was employed to keep the three-dimensional visualizations lucid and simple and wherever possible the exact anatomic relationships were preserved Practically all the illustrations were drawn in relation to bodily contours thus permitting easy ecognition of every portion of the cardiac nerve supplies in respect to the adjacent structures and to the body as a whole and furthermore thus avoiding *the unsound* practice of presenting fragments of the nervous ystem without due regard for important topographic landmarks Technical delineations necessitated taking mild liberties with dimensions and perspective but not it was hoped at the expense of accuracy The task of developing this series of anatomic *charts* was facilitated by the help of Dr L Vosburgh Lyons Attending Neurologist at the Neurological Institute

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Columbia University, and by the great skill and unfailing patience of Mrs Selina T Johnson, who put the drawings into final form

The present volume, rewritten in major part, still retains the purpose of bringing to the uninitiated as well as to the informed student a graphic visualization of the cardiac innervations, and of relating the clinical events of angina pectoris, myocardial infarction and allied conditions to the activities of central and peripheral representations of the autonomic nervous system The occasion of a new edition, however, provided a welcome opportunity to furnish a more complete account of these autonomic activities as they bear upon the body in general and on the circulation in particular Accordingly, a chapter on the general functions of the autonomic nervous system and another on the autonomic regulation of the circulation were incorporated These chapters, together with a shorter one on the anatomy of peripheral pathways were slightly modified and reprinted from the author's "Central Autonomic Regulations in Health and Disease," by the kind permission of the publishers, Grune and Stratton

It is hoped that these changes and additions will supplement a primary aim of the entire text, namely, to point up the important role of the autonomic nervous system in regard to clinical manifestations differential diagnosis, functional pathogenesis, and the medical, surgical and psychologic management of cardiac states

The past decade has sharpened the focus with which not only angina pectoris but acute myocardial infarction and allied or simulating extracardiac conditions are now regarded The present volume has therefore been expanded to cover not only angina pectoris but fuller details of the physiologic and structural events of acute myocardial infarction This explains the addition in the wording of the title of the book A chapter limited to relevant electrocardiographic illustrations containing also a discussion of electrocardiographic evidence as related to certain aspects of autonomic activity was added

Finally although there is perhaps an element of warning in the facetious observation that psychosomatic medicine is the common ground where the psychiatrist practices poor medicine and the internist poor psychiatry an attempt has nevertheless been made to put together a brief exposition of the psychologic aspects in angina pectoris and acute myocardial infarction particularly from the standpoint of the cardiologist who encounters psychogenic or psychosomatic disturbances of the cardiac apparatus No discussion of the heart maladies is entirely adequate without taking into account the emotional factors involved

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Acknowledgments

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H R M

Contents

Section Three Autonomic Pathways for Cardiac Pain

Section Four Reference, Distribution and Simulation of Anginal Pain

Section Five Concept and Mechanism of Anginal Pain

Section Six Psychosomatic Disorders of the Heart

SECTION ONE

General Clinical Aspects

CHAPTER I

General Considerations of Angina Pectoris And Acute Myocardial Infarction*

General Definitions of Terms

The term angina pectoris was originally employed to denote transient and recurrent attacks of precordial pain but more recently the term has been reserved for acute insufficiency of the coronary circulation Although in many instances this insufficiency leads to myocardial damage it seems justified at least for the present to look upon acute coronary insufficiency as a separate entity [43] and to distinguish acute myocardial infarction associated with acute coronary insufficiency and free of acute coronary occlusion from acute myocardial infarction accompanied by acute coronary occlusion This division into three conditions has validity but it must not be carried too far Clinical x ray and electrocardiographic criteria usually help keep these conditions apart but overlapping of manifestations is not rare The electrocardiographic picture of acute coronary insufficiency for example may be observed in both types of heart muscle infarction and the clinical features of acute coronary insufficiency may assume the character and magnitude of acute myocardial infarction with or without acute coronary occlusion Manifestation of (a) a generalized autonomic mass reaction and (b) the feature of anginal pain and its radiation are common to all these conditions

The cardinal features of shock precordial pain with radiation and mental anguish are decidedly more apt to occur with acute damage of the cardiovascular apparatus as opposed to acute coronary insufficiency But abrupt death may come in any of the three conditions The nature of the precipitating cause of the acute attack the predisposing factors in the victim and the sequelae which follow from somatic damage of the heart muscle or coronary vessels or in other organs vary in each individual case

* The remarks in this chapter are intended to be introductory and general a more detailed account appears in the chapters which follow

(a) *The Autonomic Mass Action*

A sudden upheaval, i e, mass action, of the autonomic nervous apparatus as a whole may be severe, intense and wide flung, or mild and subclinical practically absent The responses may be grouped as central and peripheral and consist of sympathetic (adrenergic) and parasympathetic (cholinergic) activities Disturbances in temperature regulations (fever), water balance (diuresis), sleep-waking rhythm sweating, are under central control Many cardiovascular, respiratory and gastro intestinal reactions are initiated by peripheral as well as central mechanisms (Chapter IV)

(b) *Anginal Pain and its Reference*

Anginal pain with its transmission into the usual dermatomes is, as a general rule a reliable guide in diagnosis But the pain may be atypical or it may arise in an extracardiac focus and simulate anginal pain by its overflow[45, 46] (Chapters III XI)

OPTIMAL PERFORMANCE OF HEART AND CORONARY CIRCULATION PHYSIOLOGIC FACTORS

The optimal performance of the heart depends mainly upon the normal state of the myocardium and an adequate *supply of oxygen in the blood* transported by the coronary circulation Acute coronary insufficiency is essentially the result of a discrepancy between the requirements of the heart for blood and the ability of the coronary system to deliver the blood The functional equilibrium of the heart and coronary circulation becomes disturbed when the cardiac load is beyond the capacity of the coronary system to make good or when the blood which reaches the heart is impoverished

The coronary circulation is governed chiefly by aortic pressure and the peripheral resistance of the coronary bed This peripheral resistance is influenced by (a) nervous regulation (b) the metabolism of the myocardium and (c) by mechanisms such as the strength of the cardiac contraction and variations in lymph and arteriovenous flow in the loose tissues which surround the major trunks of the coronary system (Hirsch[30]) There are also intracardiac factors contributing to the regulation of coronary flow but these are of comparatively minor significance All the factors combined achieve a flexible dynamic regulation of the coronary circuit adjusted primarily to the metabolic needs of the heart muscle The metabolic activity of the myocardium is however, the chief determinant of the amount of fully oxygenated blood required by the heart muscle and brought to it

To combat *strain upon the heart, or, better, to overcome the influence of* acute coronary insufficiency as it affects the heart, an efficient coronary circulation and an adequate supply of normal coronary blood are primary requisites

Wenckebach[42] believed that the coronary flow is actually increased in coronary occlusion, but this has no solid proof

Angina Pectoris or Acute Insufficiency of the Coronary Circulation (Acute Coronary Insufficiency)

The term angina pectoris is in many respects unfortunate It means strangulation of the chest but this describes only part of the picture and there are other objections For example the sensation of strangling may be absent and the distressed area may be distant and disconnected from the chest It would however be captious at this late date to cavil at the use of the term it has come to stay While honoring it as a label of ancient usage it has been necessary to give it a new and clearer meaning because decades of uncritical writings have piled up ambiguity and confusion not only in the employment of the term angina pectoris but also in ill assorted related designations of dubious value false pseudo mock angina

There are no false diseases there are only false diagnoses [4] and this aphorism seems especially appropriate in the study of angina pectoris. A large number of conditions it i true simulate angina pectoris but these simulations although difficult and almost impossible to distinguish at times from angina pectoris are specific conditions and not just shadow or fantom forms of angina pectoris Until comparatively recently a wide range of clinical conditions was grouped under angina pectoris at one pole the catastrophic explosion of acute coronary occlusion or sudden vagal cardiac inhibition causing swift death at the other pole various episodes of heart pain

Angina pectoris is now considered the equivalent of acute coronary insufficiency Acute coronary insufficiency as an entity separate and apart from acute coronary occlusion was recognized by many workers Danielopolu[11] stated that anginal pain is an expression of myocardial impairment *that follows from inadequacy of coronary circulation in the face of untolerated* physical strain' and that angina pectoris is due to a disparity between burdens thrown upon the heart and the failure of the coronary circulation to withstand them The same point of view was set forth by Keefer and Resnik[25] Hallermann[21] Dietrich[1] Dietrich and Schwiegk[11] [14] Buchner Weber and Haager[7] Buchner[7] Master and his co-workers[41–48] *in this* country have emphasized the recognition and significance of the condition

Concept of Acute Coronary Insufficiency

Inadequacy of the coronary system can be induced by (a) physical diminution of the coronary circulation by arterial narrowing occlusion or congenital defects collateral channels come into action but this may not be enough to uphold the equilibrium between the coronary circulation and the heart in the face of a sudden emergency (Blumgart and his associates[4] [5]) (b) reduction of coronary

flow caused by fall in aortic pressure (or by anatomic constriction of the coronary ostia) (Buchner[7]), (c) reduction of coronary blood flow as a result of nervous constriction of coronary vessels (Gilbert et al [18 19]), (d) impoverishment of the blood in the coronary circulation as a consequence, for example, of systemic loss of blood as in acute anemia (Elliott,[16] Scherf,[56 57] Master et al,[41–43]) or of poisoning of the blood from carbon monoxide (Christ,[10] Kroetz[36]), and other poisons (Wyburn Mason[64])

These conditions, however, may exist for a variable time, minutes or years, without acute insufficiency of the coronary circulation What sets it off? To understand the question, let alone answer it, it is essential to bear in mind that the cardiovascular apparatus, as is the case with other systems of the body, strives and nearly always contrives to maintain an effective functional equilibrium The adaptation between the myocardium and the coronary circulation is fundamentally an expression of what the myocardium needs and receives

Overloading the balance at either end, as from sudden or severe physical or emotional strain touches off an acute coronary insufficiency The equilibrium is thrown out of kilter and the coronary circulation already operating under difficulties, that is to say, with reduced reserve, now breaks down Acute coronary insufficiency develops and in turn may produce damage to the myocardium (Buchner [7] Neuburger [47] Opitz[49]) Again, an abrupt or major disturbance of the coronary innervations by vagal constriction following an acute loss of blood or an occlusion of a minor coronary vessel for instance, will tip the precarious balance between coronary circulation and the myocardium acute coronary insufficiency will develop and focal necroses are apt to appear in the heart wall, especially in the left ventricle (Buchner[7])

Thus far we have spoken of the train of events as it unfolds when the heart or coronary system or the blood itself undergoes a change But let us suppose as in the case of healthy young individuals, that the cardiovascular apparatus and blood are normal Can acute coronary insufficiency occur? It is difficult to answer the question categorically because it is not easy to procure correlated clinical and pathologic material with which to prove the point Acute coronary insufficiency is encountered in subjects who are ostensibly sound and normal but in them the suspicion will not down that the heart or coronary system may have been damaged in some undetectable manner after all The case cited below indicates however that acute coronary insufficiency may occur without discernible heart muscle damage and in a healthy comparatively young subject

F P a 43 year old woman with essential hypertension was operated on for detachment of the left retina and became critically ill with manifestations of acute pulmonary embolization four days later The electrocardiogram revealed signs characteristic of this state and acute coronary insufficiency She died six days later The autopsy revealed several pulmonary emboli with the heart and coronary vessels normal (electrocardiogram on p 46)

Not only in cardiovascular states but in those which involve other organs and systems disturbances in regulation may lead to severe symptoms which are however usually reversible and unaccompanied by somatic, i e structural damage But, if prolonged or intense enough the disturbance may become irreversible and thus constitute a serious threat to life or actually produce death sometimes in short order as by vagal inhibition of the frog s heart when the epigastrium is forcibly tapped On the other hand the dysregulation may go on to produce somatic damage and this eventually causes its own sequence of events reversible or not as the case may be The dividing line or zone between dysregulation of function and anatomic change is not always clear, let alone discernible This principle underlies the outcome of many disorders of the human system and the problem of acute coronary insufficiency and myocardial damage is no exception

Precipitating Agents and Factors

The most frequent precipitating agents or factors are overexertion intense emotion severe fatigue heavy or indiscreet eating and adverse meteorologic conditions Straining at stool sexual intercourse lifting excessive weights walking stairs rapid walking or running upon level ground bring on an attack also deep fatigue particularly if accompanied by hypotension Severe cold walking against a sharp wind the ingestion of heavy or large meals or excessive amounts of fluid produce attacks Attacks also come with acute loss of blood dehydration trauma to the chest or reflexly from trauma to other parts of the body Tobacco is probably an offender more so in a predisposing way (See Boyle et al[6] for effect of nicotine in inducing coronary insufficiency) Hypoglycemia the injection of pituitrin adrenalin or other sympathomimetic substances the inhalation of carbon monoxide exposure to trichlorethylene or other poisons postoperative shock the effect of anesthesia a sudden change in cardiac rhythm (paroxysmal tachycardia) heart failure and peripheral collapse are all capable of precipitating an attack Other instigators are general infections pulmonary embolization sudden dislocation of thoracic contents as in massive pulmonary collapse acute pneumothorax acute pericardial or pleural effusions a severe asthmatic paroxysm the crisis of acute thyrotoxicosis states of hypertension gout and other metabolic as well as allergic and toxic conditions All these factors fall into three groups [11-17] (1) sudden increase in cardiac work (2) reduction in coronary blood flow (3) interference with oxygenation of the blood

Unless evidence to the contrary exists it may be taken for granted that a young subject possesses a sound cardiovascular system Yet acute coronary insufficiency in such a person may be brought on as already suggested by a sudden or severe loss of blood or by shock as in post-operative situations Whether physical exertion can act in a similar way in these individuals is not

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metabolites) held responsible for pain in skeletal muscles. This analogy however, may not be altogether complete

In the first place unlike skeletal muscle the myocardium is one continuous branching system no sarcolemma sheaths each muscle fiber as is the case of the skeletal musculature An anoxic state therefore would be expected to produce the greatest and most extensive pain since the entire myocardium is affected In practice however such a correlation is not the rule Secondly the oxygen supply to the heart is safeguarded up to a certain point Below this point under the unfavorable circumstance, for example, of lowered arterial oxygen saturation the myocardium tends to be protected against the effects of anoxia by such regulatory devices as an increase in capillary oxygen utilization nervous regulation of the coronary flow changes in cardiac rate and in arterial systemic pressure and finally by intrinsic changes in the metabolic processes within the myocardial fibers This is not to gainsay however that localized oxygen deprivation of the heart muscle may occur in advanced arteriosclerotic or functional constriction (spasm) of the coronary vessels The point is that in a localized and even in some cases of more extensive anoxemia of the heart muscle an effective compensatory adaptation will tend to offset the deleterious effect of lack of oxygen Experimental and clinical observations lend support to this premise

For example in the dog Gorham and Martin[21] were able to demonstrate that pain resulted from tridirectional traction exerted on a coronary vessel in one plane the caliber of the vessel was increased and the flow through it enhanced Furthermore abrupt ligation of a coronary vessel in the dog is accompanied by intense pain Within a few hours though the *ligature is still* tight the pain may disappear although the compromised segment of heart muscle obviously still remains inadequately supplied with blood and oxygen

Clinically sudden coronary thrombosis attended by almost devastating pain is a common experience Yet, after an interval of a few hours with the thrombus undisturbed and the affected cardiac area still deprived of its normal blood supply the pain will let up and disappear Again as in the case of marked anemia or advanced luetic aortitis with almost complete closure of the coronary ostia and presumptive reduction of the blood supply to the heart cardiac pain will not be a constant feature A supplementary blood supply through intercoronary channels and arteriovenous anastomoses raises the threshold for cardiac pain yet accepting *this if* pain were due to *anoxemia* alone one would expect it to be of the utmost severity since the *entire* myocardium as one unit would be deprived of oxy*gen The fact* of the matter is, as suggested a moment ago the extent and severity of cardiac infarction is not always paralleled by the character and severity of pain A coronary thrombosis in a small or moderately sized vessel infarcting a limited portion of heart muscle

altogether clear, even though it has been claimed that marathon runners may collapse from an acute cardiac dilatation to which acute coronary insufficiency was a precursor Practitioners of psychosomatic medicine accept severe emotional strain as a valid precipitating cause In middle aged and older subjects the onset of an attack almost always presupposes that a cardiovascular derangement antedated the coronary insufficiency and contributed to it Often however, the functional derangement or the anatomic damage previously sustained may be so minimal as to deprive the heart and the coronary circulation of little if any functional capacity to meet threatening emergencies

Symptoms and Signs

Acute coronary insufficiency (angina pectoris) is generally characterized by mild episodes of evanescent chest pain cardiovascular and general systemic reactions remaining slight or minimal A disturbance in the regulation of the coronary circulation is at fault but the heart and its action may be quite good the dynamics of the circulation little deranged and the general autonomic effects minimal Fever, leukocytosis, rapid sedimentation rate and gastro intestinal symptoms are absent or inconspicuous Pain is variable, usually not intense, fatigue and some degree of prostration may set in However acute coronary insufficiency (angina pectoris) is not always so gentle a phenomenon Cardiac as well as systemic disturbances can be severe Sudden death has been known to occur even though the heart and coronary system have suffered no structural impairment The insufficiency of the coronary system is as a rule reversible, the paroxysm of the attack subsiding quickly or yielding to nitro glycerine rest and the removal of the offending or precipitating agent

Anginal pain is the most constant and perhaps most significant symptom The cause is still not fully understood Those of an archaeologic turn of mind can unearth scores of theories (Huchard[34]), but these we have deliberately avoided The present explanation of anginal pain revolves chiefly about an inability of the coronary circulation to provide an adequate amount of oxygen to the heart muscle and the hypothesis that anoxemia with resulting ischemia is the cause of anginal pain is strongly upheld by many cardiologists The theory however, is not entirely free from criticism

*Anginal Pain and Myocardial Anoxemia**

The theory that anoxemia of the heart muscle causes cardiac pain is based on an analogy of the local conditions (oxygen lack, fatigue accumulation of

* These remarks are not intended to be a complete refutation of the concept of anoxemia of the myocardium as the cause of cardiac pain but are offered merely as a critique and to point up the possibility that features other than the lack of oxygen may be significant

Acute Myocardial Infarction

Acute Myocardial Infarction Without Coronary Occlusion

Acute damage of heart muscle without the intervention of acute coronary occlusion has been a puzzling autopsy finding for many decades and the specific clinical delineations of the condition were none too well defined Gradually however it became apparent that the heart could undergo damage in relation to the coronary circulation when the latter became impaired (p 4) When the heart itself is impaired by noncoronary causes such as carbon monoxide poisoning or a marked loss of systemic blood or by disease the coronary circulation is given a task to which it may prove unequal and it becomes insufficient But whether rendered insufficient primarily or secondarily, the impairment of the coronary circulation if prolonged and severe will cause initial injury or increased damage to the myocardium This damage is disseminated in character and consists of multiple foci which go on to necrosis and then in many cases to healing

An acute lowering of the systemic blood pressure in the dog produces after a while myocardial damage This effect of lowered aortic pressure obviously is significant in connection with acute coronary insufficiency initiated by shock, hemorrhage etc (Wegria et al[62]) On the other hand with the aortic pressure unchanged and cardiac output kept presumably unaltered clamping a major coronary vessel in the dog for ten to fifteen seconds will provoke according to Green and Wegria[22] a prompt and augmented coronary flow This reactive hyperemia is induced by the local metabolic change in the heart muscle

The chief determinant in acute myocardial infarction free of acute coronary occlusion may therefore be described as physiologic in nature and related mainly to the interrelationship and interdependence between the coronary circulation and the myocardium The myocardial infarction is the anatomic evidence of acute coronary insufficiency Many investigators from the laboratory and clinic contributed to this understanding To mention a few Anrep et al[1, 3] Rein[54] Kroetz[36] Scherf[58, 57] Buchner and Lucadou[8] Buchner[7] Neuburger[47] Opitz[49] Friedberg and Horn[17] Gross and Sternberg[24] Blumgart et al[4, 5] Master et al[41–43]

Pre existing and Precipitating Factors

These are in general practically identical with those described in acute coronary insufficiency Acute heart infarction however more frequently strikes older individual and in them coronary sclerosis with or without hypertension or aortic disease are frequently pre existing factors The sequence of events is probably as follows acute coronary insufficiency is precipitated by some acute provocation abetted as it were by an underlying anatomic alteration of the cardiovascular apparatus and the acute insufficiency leads to myocardial infarction

may precipitate the most overwhelming kind of cardiac pain and general reaction

The production of pain when a human being is exposed to breathing low oxygen mixtures, as described by Rothschild and Kissin[55] and later more extensively elaborated by Levy and his associates,[38] is undoubtedly associated with an anoxic state in the myocardium However, it is not established whether an anoxic state of the cerebral centers, under such circumstances, exerts an influence on the coronary circulation in man by nerve or other pathways outside the blood stream

Although anoxemia as a factor in the genesis of heart pain can not and should not be excluded, it should be realized that certain types of intense precordial pain associated with characteristic radiations which simulate angina pectoris may be set off by excessive stimuli engendered outside the cardiac apparatus (p 221) Esophageal herniation and the severe brachial neuritis described by some French observers (Lian[39]) are cases in point

An example of anginal pain associated with esophageal hernia is that of G L a 48 year old female who was admitted several times to Montefiore Hospital She was known to have a bleeding gastric ulcer and a congenital diaphragmatic hernia and she suffered a number of episodes characterized by severe anginal pain in the lower sternal region radiating to the back and on occasions to the left shoulder In one typical attack her blood pressure rose from 168/120 to 250/138 and she developed leukocytosis The electrocardiographic tracings were always negative for signs of myocardial alteration Over a subsequent period of three years observation she showed no features of coronary occlusion or attendant heart muscle damage

In this type of case, we are most probably dealing not with a state of anoxia but with a mechanism whereby afferent stimuli from a noncardiac viscus or structure enter the neuraxis at levels linked by afferent neurons to the extracardiac organ or structure in question pain is registered in the heart and related dermatomes (p 185)

Relevant too, are the observations on the precipitation of cardiac pain by stimulating a peripheral part of the autonomic nervous system Leriche[37] brought on intense cardiac pain in human beings by stimulating the left stellate ganglion, and Spiegel and Hashimoto[60] obtained the same result in dogs That the coronary bed in man may suffer a reduction in blood flow as a consequence of functional neurogenic factors is strongly implied by the fundamental investigations on animals by Anrep and Segall[3] and by the corroborative studies of Rein[54] and Gollwitzer Meier and Krueger [0] Gilbert and his associates[18 19] observed a reduction in the coronary blood flow in dogs after experimentally induced abdominal distention and they reported the onset of pain in human beings from similar causes

Electrocardiographic findings during an attack consist of depression (sagging) of the R ST segment in one or more leads and often T inversions (p 42) The findings may disappear as abruptly as they came (Chapter III)

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Signs and Symptoms

The clinical manifestations range from mild to severe Since the general autonomic upheaval is as a rule, more pronounced than in acute coronary insufficiency, centrally initiated effects are apt to be marked Shock fever, disturbance in water balance accompanied by marked sweating difficulties in sleep, respiratory and cardiovascular or even gastro intestinal symptoms may dominate the picture, the sedimentation rate and the leukocyte count are increased The cardiovascular features are obviously of foremost significance and may be varied and mild or severe

That the clinician should long have failed to distinguish acute myocardial infarction unaccompanied by acute coronary occlusion from acute myocardial infarction associated with acute coronary occlusion is not altogether surprising since the symptoms and signs are frequently identical With a more critical approach, it became possible to distinguish these two types of infarction on the basis of the character of the pathologic lesion and the clinical and electrocardiographic features

Two points deserve special mention Trauma is held to be no factor as a precipitating cause in acute coronary occlusion, at least it is less likely and acute pericarditis and intracardiac thrombi are less frequent complications in infarction unassociated with acute coronary occlusion, because the myocardial lesion does not encroach on the inner and outer linings of the heart The last is not an absolute rule Heart failure may be an early complication or appear some time after the acute attack is over The prognosis of acute myocardial infarction uncomplicated by acute coronary occlusion is probably better than in acute heart damage accompanied by acute coronary occlusion but it would be hazardous to count too heavily on this

Electrocardiographic Findings

The electrocardiogram discloses early R ST depression which gradually returns to the isoelectric line T inversions in one or more leads and a conspicuous absence of Q waves (p 52) The signs are practically identical with those noted in acute coronary insufficiency

ACUTE MYOCARDIAL INFARCTION WITH ACUTE CORONARY OCCLUSION

Acute coronary occlusion as a clinical entity was recognized many years ago Hammer in 1878 diagnosed a case before death complete heart block was a prominent feature Dock[15] diagnosed a case before death Kent Marie[40] in 1896 and M Sternberg[61] in 1914 published accounts of acute coronary occlusion The Russians Obrastzow and Straschesko[49] in 1920 gave a careful description of the clinical and pathologic features of the condition as well as of infarction and softening of the affected heart muscle In 1911 Hochhaus[31] described 4 cases stressing the significance and course of events in acute

coronary occlusion The foremost clinical proponent of acute coronary occlusion was Herrick[7-29] his report roused the medical profession to the importance of the entire problem An extensive literature developed with many comprehensive monographs (Hochrein[32, 33] Buchner[7])

Important laboratory criteria came from Fred Smith[33] in 1918 and Pardee[31] in 1920 who described electrocardiographic signs in the onset and course of acute coronary occlusion and Blumgart and his co-workers,[4, 5] employing a specially devised injection technic carried out on autopsied hearts demonstrated the significant function intercoronary anastomoses performed as accessory or collateral channels when the coronary system or heart muscle was damaged Arteriovenous anastomoses in the coronary system proved to have a similar function (Prinzmetal et al [38]) Clinical and diagnostic criteria of myocardial infarction associated with coronary occlusion continue to receive much attention

Three main features characterize acute coronary occlusion a mechanical block in the coronary circuit an acute coronary insufficiency and an acute myocardial injury The mechanical block cannot be dislodged but accessory collateral coronary channels and newly opened arteriovenous anastomoses attempt to short circuit it the supplementation of the coronary blood supply improves the competence of the coronary circulation and promotes healing of the injured heart muscle The ability of the coronary circulation to perform at a level not below that essential for repairing the acutely damaged area of heart muscle and the state of the rest of the heart determine the fate of the victim of acute coronary occlusion

Predisposing and Precipitating Factors

Pre existing or predisposing factors consist principally of coronary sclerosis associated with or without hypertension aortitis and polycythemia[40] Precipitating factors are claimed by some to be practically nonexistent[41-43] Others like Boas[6] believe that trauma or severe physical exertion have an influence on the production of coronary occlusion Intense emotional strain indiscretion in eating and other elements are still controversial etiologic factors

Clinical Features

The acute episode and immediate subsequent course are sometimes surprisingly mild and brief More frequently the clinical picture is extremely grave death taking place at once or soon after the attack or the menace of sudden death may hover over a severe and lingering illness Systemic manifestations are quite marked as a rule and attest the severity and extent of the general autonomic reaction The general central effects observed in nonocclusive acute cardiac infarction are present here too Cardiovascular features especially anginal pain may dominate the picture especially in the beginning. Serious

Signs and Symptoms

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11 DANIELOPOLU D L angine de poitrine et l angine abdominale Paris Masson 1927
12 DIETRICH S Die Angina pectoris ein Syndrom der Ischämie des Herzens nicht Krankheitseinheit Med Welt 1933 7 42
1 DIETRICH S AND SCHWIEGK H Das Schmerzproblem der Angina pectoris Klin Wchnschr 1933 12 135
\ — AND — Angina pectoris und Anoxie des Herzmuskels Ztschr klin Med 1933 125 195
DOCK G Some notes on the coronary arteries Med & Surg Reporter 1896 75 1
ELLIOTT A H Anemia as the cause of angina pectoris in the presence of healthy coronary arteries and aorta report of case Am J M Sc 1934 187 185
FRIEDBERG C K AND HORN H Acute myocardial infarction not due to coronary artery occlusion J A M A 1939 112 16 5
GILBERT N C FENN G K AND LEROY G V The effect of distention of abdominal viscera on the coronary blood flow J A M A 1940 115 1962
— LEROY G V AND FENN G K The effect of distention of abdominal viscera on the blood flow in the circumflex branch of the left coronary artery of the dog Am Heart J 1940 20 519
GOLLWITZER MEIER K AND KRUEGER F Der Einfluss des Sympathikus auf die Koronargefasse Pflu ers Arch 1935 236 594
GORHAM L W AND MARTIN S J Coronary occlusion with and without pain Arch Int Med 1938 62 871
GREEN H D AND WEGRIA R Effects of asphyxia anoxia and myocardial ischemia on the coronary blood flow Am J Physiol 1942 135 271
GROSS H AND STERNBERG W H Myocardial infarction without significant lesions of coronary arteries Arch Int Med 1939 64 249
HALLERMANN W Der plotzliche Herztod bei Kranzgefasserkrankungen Stuttgart Ferdinand Enke 1939
HAMMER A Ein Fall von thrombotischem Verschluss einer der Kranzarterien des Herzens Wien med Wchnschr 18 8 28 97
HEBERDEN W Some account of a disorder of the breast Med Tr Coll Phys London 1772 2 59
HERRICK J B Clinical features of sudden obstruction of the coronary arteries J A M A 1912 59 2015
— Thrombosis of the coronary arteries J A M A 1919 72 365
— An intimate account of my early experience with coronary thrombosis Am Heart J 1944 27 1
HIRSCH S D l autonomie de la circulation coronarienne Quelques remarques topographiques sur les dispositifs de réglage de l irrigation cardiaque chez l homme Arch d mala dies du coeur 1947 40 433
HOCHHAUS H Zur Diagnose des plotzlichen Verschlusses der Kranzarterien des Herzens Dtsch med Wchnschr 1911 37 2065
HOCHREIN M Der Koronarkreislauf Physiologie Pathologie Therapie Berlin J Springer 1932
— Der Myokardinfarkt Erkennung Behandlung und Verhütung Dresden u Leipzig Th Steinkopff 1937 2 Aufl 1941
HUCHARD H Traité clinique des maladies du coeur et de l aorte Paris O Doin 1899
KEEFER C S AND RESNIK W H Angina pectoris a syndrome caused by anoxemia of the myocardium Arch Int Med 1928 41 769
KROETZ C Herzschadigungen und Kohlenoxydvergiftung Dtsch med Wchnschr 1936 62 1365
LERICHE R The surgery of pain Trans and ed by YOUNG A Baltimore Williams & Wilkins 1939

heart arrhythmias and sudden heart failure are ever present dangers, pericarditis and intracardiac thrombi are frequent complications since the myocardial lesion is prone to involve the pericardial and endocardial linings The lesion is generally massive, extensive and of "one piece," more homogeneous than in the myocardial infarction *unattended by acute coronary occlusion* Septal damage is frequent and produces striking disturbances in cardiac rhythm and rate

An accurate diagnosis between *acute myocardial infarction with or without* acute coronary occlusion may mean the difference between fatal outcome or recovery Acute myocardial damage without acute coronary occlusion, induced, *for example, by severe hemorrhage or postoperative shock calls for life saving* blood transfusion or vigorous antishock treatment, but these measures would be contraindicated in acute cardiac damage produced by acute coronary *occlusion*

The outcome in general varies between early or sudden death, chronic illness, and good recovery An attack may be violent or gentle but neither aspect is *a harbinger or guarantee of the eventual result*

Electrocardiographic Findings

The electrocardiographic findings are characteristic and, according to some authorities pathognomonic The R ST segment is elevated but gradually drops to the isoelectric line, T waves are inverted and cone shaped and Q waves appear (p 54)

BIBLIOGRAPHY

[1] Anrep G N Regulation of coronary circulation Physiol Rev 1926 *6* 596

[2] —— Neue Untersuchungen über Physiologie und Pharmacologie der Kranzgefasse Arch exp Pharm 1928 *138* 119

[3] —— and Segall H N The regulation of the coronary circulation Heart 1926 *13* 239

[4] Blumgart H L Schlesinger M J and Davis D Studies on the relation of the clinical manifestations of angina pectoris coronary thrombosis and myocardial infarction to the pathologic findings Am Heart J 1940 *19* 1

[5] —— —— and Zoll P M Angina pectoris coronary failure and acute myocardial infarction The role of coronary occlusion and collateral circulation J A M A 1941 *116* 91

[6] Boas I P Some immediate causes of cardiac infarction Am Heart J 1942 *23* 1

[6] Boyle M N Wegria R Cathcart I T Nickerson J I and Levy R L Effects of intravenous injection of nicotine on the circulation in normal persons and in patients with cardiovascular disease Am Heart J 1947 *34* 65

[7] Buchner F Die Koronarinsuffizienz Dresden u Leipzig Th Steinkopff 1939

[8] —— and von Lucadou — Elektrokardiographische Veränderungen und disseminierte Nekrosen des Herzmuskels bei experimentelle Koronarinsuffizienz Beitr path Anat 1934 *93* 169

[9] —— Weber A and Haager B Koronarinfarkt und Koronarinsuffizienz in vergleichen der elektrokardiographischer und morphologischer Untersuchung Leipzig Georg Thieme 1935

[10] Christ C Experimentelle Kohlenoxydvergiftung Herzmuskelnekrosen und Elektrokardiogramm Beitr path Anat 1934 *94* 111

CHAPTER II

Clinical Features of Angina Pectoris (Acute Coronary Insufficiency) and Acute Myocardial Infarction

INTRODUCTION

THE CLINICAL aspects of acute insufficiency of the coronary circulation as an isolated functional derangement yet associated with other cardiovascular events and of acute myocardial infarction with or without coronary occlusion will be considered as a whole This plan is employed to point up the common clinical and physiologic features of these conditions not losing sight of their respective distinguishing details * The symptoms and physical signs as far as possible will be discussed from the point of view of their autonomic significance

The first part of the discussion following this introduction deals with the central autonomic responses registered as disturbances in regulation of temperature water sleep-waking rhythm sweating etc and with common or overlapping pictures of these reactions as observed in acute explosive cardiac or noncardiac states The second part is devoted to an account of the divisional autonomic reactions (sympathetic and parasympathetic) responsible for the signs and symptoms associated with acute insufficiency of the coronary circulation (acute coronary insufficiency) and with acute myocardial infarction

General considerations The paroxysmal nature and unpredictability of an attack of angina pectoris (acute coronary insufficiency) are general knowledge The episode may last seconds and consist of fleeting mild precordial distress or pain or the reaction may be almost entirely emotional i e, a feeling of apprehension or impending danger or unexpected and swift death may be the first and only evidence On the other hand attacks of angina pectoris can recur over decades Severe myocardial infarction more especially associated with acute coronary occlusion is a frequent cause of sudden death Myocardial infarction with or without acute coronary occlusion can recur or come as an initial terminal event

Mild attacks These are usually due to mild episodes of acute coronary insufficiency The condition is characterized by mild evanescent pain with or without reference into the left arm and often little else except for emotional disturbance and poor sleep

* See chapters I IV

[38] LEVY R L, WILLIAMS N E, BRUENN H G, AND CARR H A The 'anoxemia' test in the diagnosis of coronary insufficiency Am Heart J 1941 21 634

[39] LIAN C L'angine de poitrine Paris Masson 1932

[40] MARIE R L'infarctus du myocarde et ses conséquences 1896

[41] MASTER A M GUBNER R DACK S AND JAFFE H L Differentiation of acute coronary insufficiency with myocardial infarction from coronary occlusion Arch Int Med 1941 67 647

[42] —— JAFFE H L DACK S AND GRISHMAN, A Coronary occlusion coronary insufficiency and angina pectoris Am Heart J 1944 27 803

[43] —— DACK S GRISHMAN A FIELD L I AND HORN H Acute coronary insufficiency an entity Shock hemorrhage and pulmonary embolism as factors in its production J Mt Sinai Hospital 1947 14 8

[44] MILLER H R The occurrence of coronary artery thrombosis in polycythemia vera Am J M Sc 1939 198 323

[45] —— The nerve pathways and clinical features of shoulder pain in relation to angina pectoris New York State J Med 1941 41 345

[46] —— The interrelationship of disease of the coronary arteries and gall bladder Am Heart J 1942 24 579

[47] NEUBURGER K Über die Herzmuskelveränderungen bei Epileptikern und ihre Beziehungen zur Angina pectoris Frankf Ztschr f Path 1933 46 14

[48] OBRASTZOW W P AND STRASCHESKO N D Zur Kenntnis der Thrombose der Koronararterien des Herzens Ztschr f klin Med 1910 71 116

[49] OPITZ E Herzmuskelveränderungen durch Storung der Sauerstoffzufuhr Ztschr f Kreislauf 1935 27 227

[50] PAL J Gefässkrisen Leipzig Hirzel 1905

[51] PARDEE H E B An electrocardiographic sign of coronary artery obstruction Arch Int Med 1920 26 244

[52] POTAIN C Des differentes formes de l angine de poitrine Gaz d Hôp 1880 53 761

[53] PRINZMETAL M BERGMAN H C KRUGER H E SCHWARTZ L SIMKIN B AND SOBIN S S Studies on the coronary circulation III Collateral circulation of beating human and dog hearts with coronary occlusion Am Heart J 1948 35 689

[54] REIN H Die Physiologie der Herzkranzgefässe Ztschr Biol 1931 92 101

[55] ROTHSCHILD M A AND KISSIN M Anginal syndrome induced by gradual general anoxemia Proc Soc Exper Biol & Med 1931 29 577

[56] SCHERF D Ein Fall von Angina pectoris Ztschr f klin Med 1932 120 715

[57] —— Koronarerkrankungen Erg d ges Med 1935 20 231

[58] SCHLESINGER M J An injection plus dissection study of coronary artery occlusions and anastomoses Am Heart J 1938 15 528

[59] SMITH F The ligation of coronary arteries with electrocardiographic study Arch Int Med 1918 22 8

[60] SPIEGEL E A AND HASHIMOTO S Über die Schmerzleitung aus dem cardioaortalen System in Beziehung zu den Spinalganglion und den Rückenmarksbahnen Ztschr f d ges exp Med 1930 71 408

[61] STERNBERG M Das chronische partielle Herzaneurysma Anatomie Klinik Diagnose Leipzig u Wien F Deuticke 1914

[62] WEGRIA R GUEVARA A R AND WIGGERS C R A study of spontaneous fulminant shock in a heart lung-dog preparation Am J Physiol 1943 138 212

[63] WENCKEBACH K F Angina pectoris and the possibilities of its surgical relief Brit M J 1921 1 809

[64] WAYBURN MASON R A new conception of angina pectoris Brit M J 1948 1 972

but among them the outstanding and by far most dramatic is the typical severe paroxysmal life-threatening oppression for all time graphically described by Heberden[14] as angina pectoris but now recognized as acute coronary insufficiency complicated by myocardial infarction with or without acute coronary occlusion

In the typical severe attack pain is no ordinary depression or discomfort instead a tremendous clutching and crushing sensation holding the heart vise like in an inexorable clasp In some cases the patient describes an iron claw grasping and tearing the heart others will live through a sensation as if a heavy bar were crushing the chest transversely at the level of the second or third intercostal spaces This torturing anguish as if life were being squeezed out is truly paralyzing so that it is not surprising that a patient so racked remains motionless in his attempt to appease his suffering The pain may stop as suddenly as it began

Pain in the heart or in the region of the heart frequently spreads in a fairly typical manner At its central point the devastating pain seems to be beneath the sternum or it may be located in any part of the breast bone The reason for this sternal localization is no clearer to the clinicians of our day than it was to Heberden[14] who confessed to bewilderment on this point From the sternum or left pectoral region pain ordinarily spreads upward curving to the left shoulder down the left arm into the elbow wrist and fifth finger thus assuming an ulnar nerve distribution At times the distribution is into the face and throat less often into the right shoulder however radiation in any direction is not constant nor is it an essential part of the picture (Chapter XI)

A sense of fullness in the chest instead of pain in the heart may be the chief complaint in angina pectoris This is not to be confused with so-called heart consciousness or with the feeling of goneness of which patients frequently complain Heart consciousness is a general descriptive term often used by patients who are undiscriminating in their choice of terms Nevertheless it expresses a degree of apprehension coupled with some kind of uneasiness localized in the heart or heart region In certain adults of middle aged and older groups this subjective complaint should always be respected even if clinical and graphic proof of cardiovascular disease is lacking This holds with even greater force for the feeling of goneness in the heart region A very troublesome symptom to conquer is the *fear of falling asleep* either shortly after coming through an attack or during a convalescent period This anxiety is really a fear of dying during sleep and is still more intensified if the subject has difficulty in breathing nocturnal dyspnea or breathlessness at any time Mental features are symptoms but mental anxiety and conflict may act to precipitate the cardiac episode

Collapse and *shock* are often striking also *immobility* of the body and the appearance of a ghastly grey color *Syncope* may occur, but more often the

Severe attacks are mainly associated with acute myocardial infarction and produce vigorous and wide spread reactions The reactions can be dramatic, terrorizing and unforgettable The onset is often abrupt, with startling pain which comes out of a clear sky, sometimes seizing an apparently healthy person, and the attack may appear for no known reason, as when the patient has been resting or even asleep Sometimes the sensation is one of severe discomfort and not genuine pain Acute coronary insufficiency (angina pectoris) occasionally produces a marked clinical response

The *incidence of fatality*, immediate or early, is supposedly small with a first attack *in young or the older individuals who have a "sound" heart and coronary* system In such individuals, Blumgart and his co workers[4, 5] demonstrated that intercoronary arterial communications, not less than 40 micra in lumen, are available for the prompt transportation of blood to the injured heart, thus bridging an emergency, and very probably the arteriovenous anastomoses of the heart, described by Prinzmetal et al, [37, 38] serve a similar purpose These anastomoses function even in hearts that have considerable coronary sclerosis When the sclerotic process has deprived the heart of the safeguard of throwing coronary anastomoses into the breach, as in advanced hypertensive arteriosclerotic heart disease, death can come with the initial infarction of the heart muscle Here, as in the advent of sudden, unexpected death which occurs by abrupt shut down of coronary ostia previously diseased by syphilis, the coronary circulation has managed by virtue of accessory and collateral channels to keep the subject seemingly well and free of pain

Although the peril of a paroxysm is unmistakable the patient succumbing often during the attack he may not only survive but live to endure, over months and years, other seizures There is, therefore much variability in the intervals between seizures and in the symptomatology of the attacks themselves even the cardinal feature of pain may be missing The predominant feature may be a gastro intestinal disturbance or a peripheral intense neuritis, *or the entire anginal syndrome may masquerade as a serious surgical condition* Whatever the form or deviations from the classic picture of the attack and how ever long the periods of remission it is unwise to be overoptimistic in prognosis *Remissions may be deceptive and recovery seldom complete Most treacherous of all* in diagnosis is the disorder free from pain "angina (pectoris) sine dolore," a condition either unrecognized or mistaken for a nonanginous condition

Both conditions angina pectoris and myocardial infarction considered as a whole are characterized chiefly by precordial pain some degree of circulatory derangement associated often with collapse and shock and by mental features of anxiety or anguish *At this juncture this triad of symptoms will be described* briefly, a fuller discussion covering all the clinical aspects is developed under the sections which deal with central and peripheral autonomic influences

Pain There are many *kinds of heart pain, varying in severity and duration*

Much milder reactions accompany an episode of acute coronary insufficiency uncomplicated by acute myocardial infarction But in any case the general character and wide distribution of the multiple manifestations which involve many systems of the body, attest the generalized mass or universal hyperactivity of the autonomic nervous system

Almost identical general autonomic reactions are observed in many acute explosive extracardiac conditions This aspect will be further discussed (p 20) The similarities sometimes make it difficult or impossible for even the best of clinician always to distinguish acute myocardial infarction for instance from acute gall bladder or pancreatic disease or from such diverse conditions as intense brachial neuritis (Lian[19]) acute esophageal herniation or acute pulmonary embolization In such circumstances the physician will come to rely for a differential diagnosis chiefly on two aids (1) the character duration and particularly the reference or distribution of pain into dermatomes and (2) appraisal of the autonomic reactions especially the peripheral manifestations with respect to their sympathetic (adrenergic) or parasympathetic (cholinergic) nature The feature of pain and it distribution we shall turn to later but at this point we shall discuss the general autonomic responses

Certain central effects such as disturbances in temperature (fever) water balance (sweating or polyuria) sleep–waking rhythm responses of the blood can not be catalogued as sympathetic or parasympathetic But centrally induced derangements of the circulation respiration and metabolism are quite readily grouped in accordance with their divisional autonomic origin The recognition of whether autonomic manifestations are central or peripheral sympathetic or parasympathetic can be of practical importance For instance states of anxiety and terror are characterized by reactions which are chiefly adrenal sympathetic shock and the state of sleep by responses which are predominantly parasympathetic Understanding these differences can be of considerable help in planning therapeutic measures

Acute myocardial infarction with or without acute coronary thrombosis is usually accompanied by fever fever is less likely and short lived in acute coronary insufficiency With the onset of heart failure particularly if the lung bases are involved or with the intervention of pericarditis or fresh infarction fever as well as leukocytosis and an increased sedimentation rate develop Disturbances in water balance are not marked unless congestive heart failure ensues polyuria excessive sweating frequent bowel movements may be evidence of a disturbed water regulation Gastro-intestinal and occasionally bladder disturbances arise and troublesome insomnia or poor sleep are rather frequent Transient glycosuria is occasionally encountered and is of central origin

Activities in various systems of the body though centrally induced can be grouped as sympathetic or parasympathetic *circulatory* responses reflected as

patient is wide awake and speechless. His facies are torn by suffering, anguish and terror with the stamp of death upon them. The victim, afraid to draw a breath, remains frozen in whatever position the attack overtakes him, helpless and rooted to the spot. He is likely to be drenched in cold sweat and salivation may be active. Breathing, restricted by pain, grows shallow and assumes a panting or sighing character, seldom Biot in type, more likely Cheyne-Stokes. Some patients become frantic with air hunger but this is not the rule. General cyanosis usually is not present; on occasions cutaneous portions of the body well supplied by capillaries take on a livid hue, i.e., lips, lobes of the ears, malar portions of the face, toes and fingers, and often become clammy. The pulse grows feeble and the blood pressure sinks.

Obviously, the human frame is not built to withstand, for longer than the briefest time, so tremendous a disturbance as is depicted above and it is not surprising that a paroxysm lasts but a very short period in actual time however endless it may seem to the sufferer. Generally the intensity of the attack wanes in a few minutes. There are cases where one such attack is not followed by another for months or years; again successive recurrences are close upon one another and of various and varying degrees of severity. Recovery too is variable, for some prompt, practically complete and lasting, for others prolonged, precarious and partial. A striking phenomenon is extreme exhaustion which may persist over days and weeks after the subsidence of the initial storm. Or, "if no accident intervenes the disease goes on to its height; the patients all suddenly fall down and perish almost immediately" (Heberden[14]).

Mental anguish or other psychic features are a frequent accompaniment of the acute attack. The terror of impending death may appear before an attack as an aura or premonition. This aura and the paroxysmal nature of the whole attack have suggested to some an epileptic character of angina pectoris (Trousseau[49]). An aura-like state of mind may accompany the paroxysm of acute coronary insufficiency or acute infarction. This state of mind is known as "angor animi" and represents a fear, at other times rather an overwhelming conviction, almost a certainty, of the approach of death. The Germans have described it tellingly as "Todesangst" or "Todesgefuhl." Often it is a true herald and death follows implacably. When the patient escapes death he has been so near it that the angor animi remains for him nonetheless a terrible and ominous experience. There are cases in which it is almost the sole subjective symptom, Allbutt[1] wrote, "it chiefly consists in this."

I. General Systemic Reactions Induced by Mass Action of the Autonomic Nervous System

A galaxy of widespread and vigorous central autonomic reactions is usually evoked by the severe attack of acute myocardial infarction which occurs with a sudden closure of a coronary vessel or even without the latter complication

In the ri ht lower quadrant there was moderate tenderness and some pasm of the right rectus mu cle especially of the lower half The temperature ranged between 101 and 10 F The blood count showed 17 600 white cells, 89 polys (41 stab forms) The patient was pale per pired profusely and looked acutely and gravely ill He was in shock and mentally greatly agitated by fear of death A laparotomy promptly carried out disclosed a normal looking appendix it was removed On section it showed only mild chronic changes The temperature remained at about 101 F for about six ubsequent days then became normal In this case the local features pointed strongly to an acute gangrenous appen licitis an l were accompanied by a marked autonomic general reaction yet no somatic damage was uncovered either at operation or durin the subsequent and uneventful course

(3) *Acute ch lecystitis* A young woman 2? years old always in good health an l married for two ears the mother of a child one year ol l became very ill within a few hours She developed fever 10?–103 F ions of collapse sweating and some nausea. Her abdomen was soft, not spastic or distended and no tenderness was elicitable She gave the impress on of being very .i k and had it not been for her youth and the excellent condition of her car liovascular ys tem a diagnosis of acute coronary occlusion might have been seriously entertained despite the absence of precordial pain She was su pected of having a sudden explosive con l ti n in the abdomen and either an acute cholecystitis or a duodenal perforation Laparotomy on the fo lowing day revealed a very large gallbladder the mucosa of which ha l alre ly u ler gone patchy necrosis The organ was disten led with cloudy flui l not yet frankly purulent Recovery was excellent and permanent

Averbuck has reported two interesting cases of acute generalized postoperative peritoni tis simul tin, acute coronary thrombosis

(4) *Cereb al ap plexy* L L 8 years o d ha l been under observation for about 10 years For this period she was know n to have a systolic and dia tolic hypertension of about 2?0 1?0 Except for some difficulty in her vi ion due to vascular changes she had enjoyed an active and rather well rounded life She was su ldenly stricken with a left hemiplegia accompanied by the immed ate onset of marked shock fever (10? 103 F) profuse drenching sweats an l vasomotor disturbance of the kin The latter took the form of su lden an l intense copper hued flu hing f the face an l upper torso including the upper extremities This coloration w ul quickly chan e to a violaceous hue and after ten to fifteen minutes return t normal Similar peripheral manifestations were noted in other parts of the body an l the involvement was never patchy but conformed fairly closely to segmental level She showed also a disturb ance in the leep–waking rhythm and within a few weeks glycosuria appeared

(5) *Acute pulm nary emb li ati n* K M 81 years ol l had enjoyed excellent health all her life For about fifteen years she had varicose ein of the lower limbs more marked on the ri ht ide With ut any apparent cau e she suddenly developed seizures of intense precordial pain marked collap e as ociated with feeble thready pulse low bl od pres ure (100 6) profuse sweating and mental angui h Within a period of three months she experienced eight seve e and several minor episodes of this character In the intervals between the attacks he slowly re overed thou h not completely Physical igns of pulmonary involvement became mor pronoun ed but signs of circulatory failure did not supervene A d agnosis of recurrent pulmonary embolization wi h pulmonary infarction was made and the varicose veins of the right si le (because of local changes in this limb) were considered the site of origin of the emboli The ri ht saphenous vein was ligated and di ided at the femoral triangle Thereafter no fur ther embolizations took place She is now 92 years old and in good health The repeated elec trocardiograms disclosed no heart disturbance

change in blood pressure, heart rate or output, *respiratory* reactions expressed as alteration in rate, rhythm or pattern of breathing, *gastro intestinal* symptoms which take the form of meteorism, diarrhea, abdominal colic, *genito urinary* manifestations announced mainly as kidney or ureter symptoms *sweating pilo motor reactions, etc* These manifestations do not originate in the autonomic ganglia and neurons outside the neuraxis as in the case of change in heart rate produced by stimulating or depressing the peripheral cardiac innervations

Shock, emotional fear, anguish and other features of acute cardiac as well as extracardiac episodes, are central autonomic manifestations Pain, too, is almost a constant element in all these episodes but it is more strictly a peripheral manifestation The registration of pain into consciousness by the thalamus and cortex is a central process but the mediation of pain is accomplished by peripheral pathways

CLINICAL EXAMPLES

The group of cases below illustrates the variety of ways in which the autonomic nervous system reacts en masse The clinical manifestations may vary in pattern or in degree of intensity, not only in acute conditions but in subacute or chronic states as well But the clinical manifestations excluding those directly due to somatic damage, are always expressions of an autonomic discharge When confronted by any of these clinical conditions the physician will recognize *that the attendant features of shock lowered blood pressure, slowed heart* rate prostration, meteorism, vertigo etc are parasympathetic in character, and that sweating pilomotor reactions unusual elevations in blood pressure and tachycardias are sympathetic All the manifestations central and peripheral are marshalled promptly and effectively as for an emergency

(1) *Reaction to ingested spoiled food* J S a business executive 58 years old with mild diabetes but otherwise in rather good health complained toward the close of a work day of some nausea and general malaise he refused his dinner Within an hour he was in severe shock The skin became grey and cold to the touch the entire body was covered with perspiration His blood pressure usually at 130/80 fell to 85/50 the pulse grew very weak and at times imperceptible The patient was prostrated and although apparently a restrained and unemotional individual he stated that he felt his end was near *Despite the absence of precordial or referred* anginal pain he gave the appearance of having suffered an acute occlusion of a major coronary vessel his condition was alarming and his chances for survival seemed poor Within two hours however and without the administration of any medication except a small dose of morphine *the blood pressure returned to normal levels* the pulse became full and strong the skin rosy colored and the exhaustion disappeared An electrocardiogram taken the next day was normal He resumed his work after resting another day Subsequently it was disclosed that the patient and his brother had partaken of some spoiled food at lunch on the day of the attack and that the brother had also developed practically the same reaction

(2) *Acute gangrenous appendicitis* D C 58 years old in good health developed (at 3 a m) intense abdominal pain especially on the right side the pain persisted unrelieved for five hours

infarction The jaundice steadily deepened and a tender gall bladder mass became palpable Fever and leukocytosis persisted the temperature ranging from 101 to 103 F on the tenth day Surgical opinion held that the primary condition was either acute pancreatitis or acute cholecystitis Laparotomy revealed an acute but resolving cholecystitis The patient succumbed to a fresh cardiac attack on the day after operation and autopsy disclosed an acute cholecystitis with areas of resolution a recent infarction of the posterior wall and a recent thrombosis high up in the left descending coronary vessel

No experienced physician has failed to encounter similar cases in which the manifestations of acute explosive states constituted a violent reaction of the autonomic nervous system Chapter XII on simulations furnishes many extracardiac examples Since acute coronary insufficiency occurring without myocardial infarction and acute myocardial infarction with and without acute coronary thrombosis may have enough common autonomic reactions to make clinical differentiation very difficult it is suggested that a classification which considers these three cardiovascular conditions always separate entities is perhaps too rigid

II Autonomic Divisional Manifestations

The individual manifestations as well as the total clinical picture of acute explosive states such as acute coronary insufficiency or acute myocardial infarction consist of responses by each autonomic division The responses may be predominantly sympathetic or parasympathetic since each division does not necessarily react with equal magnitude or extent

During an attack of acute myocardial infarction for instance the parasympathetic division as already mentioned may depress the blood pressure and even tend to retard the heart slow the respiration induce meteorism vomiting nausea (the nausea presumably is a sensory vagal effect) and bring about localized vagal motor phenomena such as constriction of the coronary vessels the bronchial musculature or muscles of the throat or epigastrium These parasympathetic effects however may be overshadowed or never allowed to develop when the hyperactivity of the sympathetic division gets the upper hand Sympathetic (adrenergic) responses become prominently manifested as respiratory acceleration generalized sweating activity occasionally including pilomotor reactions and vascular responses which may include hypertension of some circuits i e the peripheral vascular bed tachycardia etc Sweating is centrally induced by central sympathetic representations but is registered by parasympathetic postganglionic neurons

A Sympathetic Manifestations

1 *Cardiovascular Features*

Cardiovascular features in acute coronary insufficiency (angina pectoris) may be mild negligible or absent Pain and reference into dermatomes can be an outstanding feature but the heart sounds hardly change the cardiac output

(6) *Esophageal herniation* M C aged 54 was admitted to Montefiore Hospital in 1940 It was alleged that he had had an acute coronary occlusion in 1930 With the onset of that attack which lasted several days he experienced dyspnea and intense cutting pain across his lower chest Thereafter up to the time of his admission he had repeated seizures of severe paroxysmal dyspnea and intense precordial pain brought on by excitement or undue exertion as for instance on walking up a flight of stairs In the last year the attacks were accompanied by darting pain in the left shoulder radiating down into the left arm leaving a sensation of numbness in the arm Frequently the pain was associated with a sensation of suffocation Throughout these years he developed no congestive failure More recently attention was directed to his gastro intestinal tract because of features suggestive of peptic ulcer The x ray studies disclosed an esophageal herniation The episodes which in recent years at least simulated attacks of sudden coronary occlusion were due to the herniation and not to any somatic damage of his cardiovascular apparatus For more than 11 years he had failed to show clinical or electrocardiographic evidence of cardiovascular disease

(7) *Acute coronary insufficiency induced by a heavy meal* A heavy set swarthy Italian individual A B aged 48 developed promptly after the ingestion of an unusually rich and heavy meal late at night intense precordial pain radiating into the left arm and shoulder accompanied by marked collapse The blood pressure fell from normal levels of 128/88 to 80/50 the pulse became imperceptible and dyspnea was marked This acute alarming episode disappeared within a few hours and the patient was ambulant and apparently well His blood pressure was restored to normal within a day He was known to have had mild anginal pain in the past

(8) *Acute myocardial damage without coronary occlusion* M C a 46 year old heavy set polycythemic individual was suddenly seized following an intense emotional upheaval with severe precordial pain pallor which gave place to cyanosis vertigo profuse sweating and general collapse His blood pressure which had steadily mounted in the previous year to 190/120 dropped to 150/80 An especially troublesome manifestation was recurrent anginal pain accompanied by sensations of suffocation Congestive failure did not appear The electrocardiogram disclosed signs of acute myocardial damage

(9) *Anterior wall infarction with acute coronary occlusion* J J a 68 year old male with symptomless generalized arteriosclerosis and hypertension (190/120) the latter of several years duration suddenly developed intense precordial pain radiating into the left arm The seizure was quickly followed by shock cyanosis depressed blood pressure (90/65) feeble pulse volleys of extrasystoles marked prostration temperature of 102 to 103 F and leukocytosis The cardiac arrhythmia never developed into paroxysmal tachycardia Frank congestive failure did not appear but recurrent anginal pain and prostration lasted many weeks The electrocardiogram taken about ten hours after the attack revealed characteristic signs of acute anterior wall infarction associated with acute coronary occlusion

(10) *Posterior wall infarction with acute coronary thrombosis and acute cholecystitis* L M 68 years old in excellent health for years was seized soon after an evening meal with agonizing upper epigastric and precordial pain Shock and cyanosis appeared promptly the cyanosis persisting even while he remained in an oxygen tent During the next four days he had recurrent episodes of severe precordial pain associated with bloody frothy sputum also attacks of cardiac collapse and recurrent episodes of transient auricular fibrillation The electrocardiograms on the second eighth and sixteenth days disclosed signs of acute infarction of the posterior wall associated with acute coronary occlusion Five days after the onset of his illness he ... attributed at first to pulmonary changes attendant upon

the sensation of pain projected into the cardiac territory as a psychosomatic symptom the coronary circulation is not involved (Chapter XV)

In the classic severe attack of acute myocardial infarction the pain may be very severe and is always fraught with grave danger but the peril may be as great with mild pain or even in the absence of pain (sine dolore) Heart weakness collapse the angor animi' and a history of similar episode with or without pain bear witness to the diagnosis What is true of the intensity is also true for the duration A fleeting pain severe or mild may bring death although as a rule fleeting pains are recurrent and not always alarming All this emphasizes the variability of the nature and other aspects of anginal pain and the danger that lurks even in its mildest manifestations

The character of anginal pain is not uniform This is well demonstrated by the ways in which it is described boring burning crushing bursting twisting tearing knifelike lancinating viselike clawlike or dull oppressive leaden etc Most of these terms apply to pain of a mechanical character Some patients among them well trained physicians have unmistakably described some of these mechanical types of agony i e insupportable weight on the chest as if the sternum were being crushed back to meet the spine There is no mistaking the agonizing unbearable character of this pain in a full fledged intense attack but the descriptions of pain may vary in the same individual from one attack to another as may the intensity or duration of the pain There are slight minor attacks and still milder forms shading off into states of distress or uneasiness Slight exertion cold emotions are capable of producing minor attacks These have been compared to and even named petit mal of angina and they may be as ominous as the vicious horrible variety the milder pains differing from the other types in degree only Pain as already mentioned is conspicuously absent in the type named angina (pectoris) sine dolore and exitus with this is by no means unknown When a first attack of angina (pectoris) sine dolore is not fatal recurrences are not unlikely the paroxysms possessing some or all of the other features heart weakness collapse and terror met with in the painful variety

Vaquez[60] has made a special point of dividing anginal pain into that brought on by effort (effort syndrome) and anginal pain without effort (decubitus) The latter was further subdivided by Danielopolu[7] into anginal pain of repose that is when at rest in the waking state usually in the daytime and anginal pain during the night This classification is open to objection Vaquez[50] claimed that the anginal pain and associated features which occur during rest in bed (decubitus) or even in sleep represent a spontaneous failure of the left ventricle effort playing no part in producing the failure But this takes it for granted that during sleep the body is devoid of fluctuations in metabolic activity or emotional content This is far from the fact and these processes indeed may be equivalent to effort thrown upon the heart and coronary circulation The transient charac

is rarely affected and the heart rate remains normal or perhaps moderately accelerated The blood pressure, too, is little disturbed and heart failure is not expected Peripheral collapse and shock are seldom part of the picture Syncope is sometimes a feature and not to be confused with uneasiness or mild mental confusion, manifestations which usually are preliminary to an attack Prolonged or progressive coronary insufficiency can lead to very severe manifestations, including heart failure and death, more often myocardial infarction intervenes and contributes to the outcome Sudden or unexpected death fortunately a rare event in acute coronary insufficiency (angina pectoris), may be the only clinical testimony of acute coronary insufficiency the autopsy disclosing either extensive subendocardial necrosis or hardly any lesion if death is early

The cardiovascular features, as we shall see, are generally more marked and intense with the advent of acute myocardial infarction

(a) *Anginal Pain* It may be asked whether pain is properly grouped as a sympathetic manifestation since the afferent pathways for pain are not considered part of the autonomic apparatus For the clinician, however, this is an academic point Pain has been grouped with sympathetic reactions for two reasons because pain or its associated effects are transmitted centrifugally by efferent sympathetic fibers, causing for example peripheral vasomotor or sudomotor responses and because the surgical attack on anginal pain is directed largely to interrupting the efferent supplies to the cardiovascular apparatus

A connection between the segmental dermatomes and the neuraxis is laid down early in embryonal life A portion of the outer integument develops into the central nervous system, the skin forever preserving its neurogenic property, and the viscera become connected to the dermatomes by nerves which pass through the neuraxis This connection is the basis for the dermatomic reception of pain arising in the heart and other organs The pain is sometimes wholly confined to the reference zone In man pain and its reference serve as a grim albeit beneficent warning signal

The heart is supposed to be an insensitive organ a belief which is supported by authentic records of injury to the heart from external causes such as knife stab etc Most cardiac conditions other than acute coronary insufficiency and its allied complications are free of heart pain Thus disease of the heart muscle the endocardial lining the valves the nodes junctional and septal structures rarely produces pain Exceptions are rheumatic mitral disease especially in a small percentage of children and occasionally in an adult and rheumatic aortic disease anginal pain appears more frequently when the etiology is luetic Cardiac pain sometimes occurs in cardiovascular disease associated with marked hypertension Heart pain is seen in hypertensive states in anemias and other blood conditions in Graves disease in toxic states (poisons) pericardial pain is excluded in this discussion The pain may be caused by mental conflict

pain with incapacitation and even to sudden, unexpected death This occurs upon the advent of exertion or other precipitating elements acting upon a cardiovascular system that would otherwise be expected to carry on for years On the other hand patients with a marked diminution of cardiac reserve due to antecendent crippling attacks of coronary or heart disease may weather fairly severe attacks characterized by intense anginal pain

Some of the unpredictability in the relationship of the degree and extent of an acute cardiac attack and the amount of effort or other precipitating cause is due to the fact that we have no accurate method of measuring untapped and unused cardiac reserve Nor can we estimate precisely how much of this reserve is brought into action in the face of effort nor how capable the coronary circulation will prove to be in putting into use collateral interarterial channels of 40 micra or more or arteriovenous anastomoses In short even when pre-existing cardiovascular damage is suspected it cannot always be recognized let alone gauged It therefore happens and with tragic consequences that a mild apparently insignificant exertion i sometimes enough to tip the scale and bring on severe anginal pain and even dissolution Effort therefore however trivial it may seem to the victim must be avoided if it has been known to produce anginal pain or related features

The same individual may vary in his tolerance to effort that is to say without demonstrable change in the cardiovascular system he may negotiate stairs at one time without difficulty and at another time the same performance is impossible or disastrous As nearly as one can tell no known factors have been introduced to explain the difference in reaction Undoubtedly the tolerance varies with the physiologic endowment of the heart and coronary circulation but this can be measured and evaluated in a gross way only

Just as effort frequently brings on an attack of acute coronary insufficiency stopping the effort will often stop the attack This is particularly so in seizures of rather mild anginal pain The effort syndrome is characterized by the provocation of pain associated sometimes with dyspnea and even mild effort may be an offender Stopping the effort enables the patient to get his second wind and he then proceeds in comparative comfort if the exertion ahead is not too taxing This is almost a pathognomonic sign of acute coronary insufficiency (angina pectoris) In the face of a mild effort such as climbing a gentle slope mounting a few steps or even traversing a city block or two the heart promptly flags and its owner develops breathlessness pain in the precordium possibly with overflow manifestations This brings him to an abrupt halt Some who shun any demonstration of illness pretend at window shopping (Schaufenster Krankheit) The physical exertion is b aked and an immediate physiologic adjustment takes place whereby the left ventricle has an opportunity to become stabilized The patient now without fear and the heart without pain can resume and finish the appointed task Although the genesis and mechanism with

ter of these types of anginal pain attest to the temporary nature of the disturbance in the coronary circulation, i e, acute coronary insufficiency This contrasts with severer and more enduring anginal pain produced by acute myocardial infarction

Slow moving arteriosclerotic changes in the blood vessels of the heart lead to constriction of their lumen and to obliteration, but these gradual changes are not attended by pain On the other hand, it is comparatively rare for abrupt or sudden occlusions in the coronary vessels not to cause pain The sensation varies from extreme anguish to mild distress or none at all, depending upon the many physiologic and psychologic elements such as the individual's *threshold for the perception of pain*, etc The chief consideration, however, is undoubtedly the heart itself, its age and condition in respect to the vascular supply to the musculature in respect to the caliber of the vessels and especially to the capacity of the organ to call upon collateral channels to protect the distressed areas

The pain in all these conditions is localized in the heart or in the region of the heart Of the authenticity of this localization, i e, in or about the heart, not only the testimony of sufferers but the records of careful clinical observers leave no room for doubt It is therefore open to some question whether the heart is truly an insensitive organ The coronary vessels in lower forms are known to cause pain, but in human beings this information is lacking (Spiegel[44-48])

Although angina pectoris (acute coronary insufficiency) often includes more than pain and pain, in fact may be absent, it may be the single feature of an attack and thus practically synonymous with angina pectoris Anginal pain has fairly well defined delineations, even though graduations and nuances of the pain modalities, variations in distribution and reference reversals in the direction of the distribution and substitutes or equivalents have been described [9] While anginal pain in uncomplicated acute coronary insufficiency (angina pectoris) may not be outstanding its physiognomy takes on new proportions when the insufficiency is accompanied by acute heart muscle damage or by acute coronary thrombosis with infarction of a related myocardial area Anginal pain on the other hand, is alleged to be warded off by congestive heart failure This is not always the case nor is it consistently valid that the attack of acute coronary insufficiency which instigates anginal pain will not come off in the presence of auricular fibrillation

(b) *Anginal Pain and Effort* The connection between anginal pain and effort is common knowledge and exemplified in many cases Effort is the most frequent precipitating cause of acute coronary insufficiency plays a part in producing acute myocardial infarction and is perhaps not entirely excluded as a precipitating factor in acute coronary occlusion Not always is there a quantitative relation between the onset or degree of the cardiac episode and the amount of physical exertion Thus seemingly insignificant exertion may lead to anginal

duce severe and even alarming features As the minute output is reduced the circulation may develop forward failure, i e not enough blood reaches the peripheral circulation The acute form of this type of failure can produce a picture which resembles shock (peripheral vascular failure) with manifestations of weakness fatigue fall in blood pressure cold clammy skin and unconsciousness Sudden weakness of a severely infarcted heart or heart failure induced by severe unrelieved tachycardia as in acute coronary insufficiency, for instance may produce peripheral vascular failure The peripheral failure is associated with reduction in cardiac filling diminished coronary flow and undernutrition of the heart muscle Peripheral vascular failure also has been attributed to a reflex act and not directly to the state of the heart muscle or the character of coronary flow Although cardiac output appears to be undisturbed in many cases of acute coronary insufficiency the patient often experiences lassitude fatigue weakness or faintness and for days or weeks after the acute episode is over the complaints may persist Whether these symptoms represent after all some form of undetected impairment of cardiac output cannot be said Recovery is usually rapid and complete and the cardiac output if it has been disturbed is quickly righted Prolonged or extremely severe coronary insufficiency can reduce the cardiac output and so lead to the manifestations associated with forward failure

Cardiac Output in Acute Myocardial Damage The cardiac output as a rule is diminished when the heart failure is associated with myocardial *infarction* (Hickam and Cargill[15] Stead et al[17]) complicated by congestive manifestations Undiminished and even increased cardiac output has been noted in congestive heart failure in subjects with thyrotoxicosis anemia or *beriberi* and this paradoxical result is explained by the fact that the cardiac output is *augmented* before the onset of congestive heart failure and that the cardiac output is depressed but not to subnormal levels

Cardiac output and congestive heart failure are *to a* great degree conditioned by the state of the myocardium As the left ventricle weakens back failure develops The feeble left ventricle permits the pressure to rise in the left auricle and the pulmonary circulation as a consequence is retarded and the pulmonary vessels become engorged *and stiffened* Vital capacity is diminished and breathing rendered difficult The difficulty in breathing or dyspnea is due to the effect of local congestion on pulmonary vagal endings and not to chemical agents acting on the respiratory centers As volume and pressure in the pulmonary circulation increase the right ventricle will eventually weaken still more the systemic venous pressure will rise and visceral engorgement and general edema ensue

The accumulation of fluid (edema) *in* the organs and tissues is attributed mainly to two factors (a) a reduced renal flow which follows lowered cardiac output (Warren and Stead[14]) and (b) the diminished reabsorption of sodium

attendant pain are not entirely clear, the achievement of a "second wind" represents a very useful warning to the anginal patient and enables him in certain physical tasks to avoid threatened disaster. By trial and error, the intelligent sufferer comes to realize the limitations which surround him and he will undertake certain efforts with the greatest circumspection and shun others entirely. But this is not a universal rule, for the most intelligent patients may be unsuccessful.

The effort involved for instance in many bodily functions is a serious problem to some patients. Swallowing, voiding, mastication, defecation, sexual intercourse, speaking, sneezing, coughing, retching, acts which are only in part under conscious control and, therefore, almost passive functions, may bring on anginal seizures. In advanced cases the effort entailed even in the mildest of these acts is sufficient to usher in a paroxysm: lifting an easy weight such as a small grip, stooping to the floor or rising from a chair or from bed, very slow walking, especially in the face of a wind or in the presence of cold. Even speaking at some length in an ordinary tone of voice or the performance of light hand work while at rest may lead to an anginal attack. Deep sighing, yawning or a sense of leaden weariness may be in the picture. Apart from the emotional excitement entailed, a sudden trauma under other circumstances almost inconsequential as such an injury as stubbing a toe, bruising a finger nail, or even being shaken in a moving vehicle may be a precipitating cause. The physical effort in all these active and passive acts is not always the same, which explains in part why they are not always precipitating causes.

Less frequent but not at all rare is another form of effort syndrome signalized by a delayed yet sudden onset of deep weariness, sighing and yawning, some degree of shortness of breath, and heart or precordial pain radiation into the left arm is sporadic. This train of events comes on minutes, sometimes ten or fifteen, after, not during, the expenditure of an effort. The postponed reaction may overtake the subject when he is resting and the performance of exertion forgotten. He must be on guard, therefore, against overtaxing himself during the period that follows an exertion. The mechanism probably is related to oxygen debt.

(c) *Cardiac Rate.* Sinus tachycardia is frequent, especially in acute coronary insufficiency. Supraventricular or ventricular paroxysmal tachycardia, auricular fibrillation, auricular flutter, extrasystoles, heart block may accompany myocardial injury. Changes in heart rate are not necessarily of serious import. A very rapid rate, however, in a badly damaged heart adds to the gravity of the situation. Bradycardia, on the other hand, is not frequent in myocardial infarction and is, indeed, considered a favorable sign (p. 35). Pulsus alternans is a grave sign if the heart rate is not too high.

(d) *Cardiac Output in Acute Coronary Insufficiency.* The inability of the cardiac pump to deliver adequate amounts of blood to the tissues of the body may pro

duce severe and even alarming features As the minute output is reduced the circulation may develop "forward failure", i e not enough blood reaches the peripheral circulation The acute form of this type of failure can produce a picture which resembles shock (peripheral vascular failure) with manifestations of weakness fatigue fall in blood pressure cold clammy skin and unconsciousness Sudden weakness of a severely infarcted heart or heart failure induced by severe unrelieved tachycardia as in acute coronary insufficiency, for instance may produce peripheral vascular failure The peripheral failure is associated with reduction in cardiac filling diminished coronary flow and undernutrition of the heart muscle Peripheral vascular failure also has been attributed to a reflex act and not directly to the state of the heart muscle or the character of coronary flow Although cardiac output appears to be undisturbed in many cases of acute coronary insufficiency the patient often experiences lassitude fatigue weakness or faintness and for days or weeks after the acute episode is over the complaints may persist Whether these symptoms represent after all some form of undetected impairment of cardiac output cannot be said Recovery is usually rapid and complete and the cardiac output if it has been disturbed is quickly righted Prolonged or extremely severe coronary insufficiency can reduce the cardiac output and so lead to the manifestations associated with forward failure

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Cardiac output and congestive heart failure are to a great degree conditioned by the state of the myocardium As the left ventricle weakens back failure develops The feeble left ventricle permits the pressure to rise in the left auricle and the pulmonary circulation as a consequence is retarded and the pulmonary vessels become engorged and stiffened Vital capacity is diminished and breathing rendered difficult The difficulty in breathing or dyspnea is due to the effect of local congestion on pulmonary vagal endings and not to chemical agents acting on the respiratory centers As volume and pressure in the pulmonary circulation increase the right ventricle will eventually weaken still more the systemic venous pressure will rise and visceral engorgement and general edema ensue

The accumulation of fluid (edema) in the organs and tissues is attributed mainly to two factors (a) a reduced renal flow which follows lowered cardiac output (Warren and Stead[24]) and (b) the diminished reabsorption of sodium

by renal tubules (Merrill[5]) These explanations are, perhaps, not entirely free from criticism *In the first place, some waterlogged patients with congestive* heart failure show a normal or even increased cardiac output, in the second place, it is difficult to reconcile waterlogging of the body on the basis of disturbed tubular reabsorption with the experience that waterlogging is absent when the tubular apparatus is crippled by nephrosclerosis

The average cardiac output of normal adults at rest is approximately 5 4 liters per minute or 3 1 liters per square meter of body surface (Cournand[6], Warren and Stead[54] McMichael and Sharpey Schaefer[4]) The output may be reduced 50 per cent or more in heart failure associated with cardiac anasarca These results have been recently obtained by the intracardiac catheterization technics based as were the older methods on the principle of the direct Fick method A caution is in order on evaluating the recent data, the normal cardiac output is reduced almost one third when the subject assumes a recumbent position [4]

(e) *Coronary Circulation* The degree and extent of dynamic alteration in the coronary circulation of human beings has not been directly established because the technical difficulties have been insurmountable A considerable body of information of the physiology of this circuit has nevertheless been obtained by investigations on lower forms Recently, Goodale et al[10 11] succeeded in catheterizing the coronary sinus of dogs and this has led to a similar technic in man (Bing et al[3]) This points to a direct method of investigating heart muscle metabolism and of determining the energy output (wattage) of the heart as a pump

On theoretic principles if the coronary flow over a given time were known, the work of heart muscle could be calculated by noting the difference in temperature between afferent and efferent blood Since a method for determining the coronary volume in man has been made available by Kety and Schmidt (Am Heart J *1949 38* 1) it may prove feasible to correlate temperature gradient and blood flow utilizing the former as an index of cardiac metabolism Then too the employment of isotopes contrived with a specific linkage to elements which participate in the intermediary metabolism of heart muscle might yield information on the efficiency of the heart as a pump It is known for instance that anoxemia leads to profuse disturbances of crucial points in the long chain of intermediary metabolic activity and a disturbance of this type i e pyruvemia has been correlated with the degree of heart failure (Yanof[55]) and with abnormal T waves (Randles et al[39]) Methods of the type suggested above are obviously not perfected and the functional impairment of the cardiac apparatus in acute coronary insufficiency or acute myocardial infarction is at present evaluated chiefly by clinical x ray and electrocardiographic criteria, methods which leave much to be desired

(f) *Pulmonary Circulation* Cardiac output in acute coronary insufficiency and in acute heart muscle damage is tied up with the regulation of the pul

monary circulation since this extracardiac circuit is the first to bear the brunt of the dynamic changes initiated by damage to the pump (heart)

A sharp rise in pulmonary blood pressure is alleged to accompany angina pectoris (acute coronary insufficiency) occasionally in marked hypertensive individuals Sahli[40] proposed his "Hochstauungsdruck" theory to explain such a rise maintaining that in the pulmonary circulation the blood pressure heightened by long standing hypertensive cardiovascular disease underwent abrupt variations responsible for sudden attacks of pulmonary edema and that the latter evoked reflex constriction of the pulmonary vessels This explanation is however theoretic The pulmonary circulation of nonhypertensive individuals is also though very infrequently subject to bursts of elevated blood pressure Not only were these and other activities of the pulmonary and cardiac circulations looked upon as reflex in nature but a reflex it was held governed the interaction of both circuits (Struell[41] Villaret et al[42, 43]) Scherf and Schonbrunner[44, 45] offered electrocardiographic evidence to support this latter contention but this evidence Parin[35] *maintains is not conclusive The electrocardiographic signs resembling myocardial infarction observed in acute pulmonary embolization may be due he feels to depressor effects on the systemic circulation and to alterations in gas exchange which in turn affect the coronary circuit* *

(g) *Blood Pressure* Uncomplicated acute coronary insufficiency disturbs *the* arterial blood pressure little A sudden rise in systemic pressure is *observed* occasionally in hypertensive subjects in the *early stage of acute myocardial*

Speculation is perhaps in order whether the pulmonary artery possesses sinus receptors which help *regulate the* systemic and pulmonary *circulations* Evidence to support such a contention *consists of the striking analogy in lower forms* and in the human embryo *of the* regulative functions of the depressant sensory receptors in the branchial arteries and of relevant clinical observation in *human* subjects

The branchial arteries associated with the branchial arches in aquatic forms possess *nerve* elements which participate in regula*ting the circulation and respiration* Similar elements or receptors are recognizable in all the branchial arteries of the mammalian embryo Before birth however the first and second set of arches *atrophy the third* set forms the carotid vessels with their retained receptors the fourth (*on the left side*) becomes the aorta with its sinus receptor the fifth and sixth sets fuse into *the pulmonary* artery Receptors *in the* pulmonary artery would therefore be *expected* to survive and function

Parin[35] on *the* basis of his own *studies and* the work of predecessors states that the pulmonary artery branches possess dep*ressor receptors* which following a local increase in pulmonary blood pressure induce a (dep*ressor*) fall in systemic blood *pressure* and a slowing of the heart rate The influence *of these receptors* on the pulmonary blood pressure has however not been investigated

It is rather remarkable that *death* from acute massive pulmonary embolization and infarction is practically instantaneous and *signs of* asphyxia seldom part of the picture These observations are highly sugg*estive* of the activity of a powerful reflex depressor effect produced by the pulmonary receptors *in a manner* analogous to the swift death known to follow stimulation of the carotid or aortic sinuses.

damage, and in nonhypertensive cases the rise is even less frequent The elevation is mainly in the systolic level, the diastolic plateau remaining less volatile and the episode is transient

Since the early stage of acute myocardial infarction is characterized by a parasympathetic (depressor) effect, it seems paradoxical to find even rarely a sudden elevation of blood pressure When it is realized, however, that both autonomic divisions may be hyperactive with the onset of the autonomic upheaval, it will not be surprising to find that the sympathetic occasionally gains the ascendant role

Venous pressure is greatly increased in congestive heart failure, especially in chronic failure The increase takes place after considerable salt and water have been retained and the blood volume has increased (Warren and Stead[34]) This train of events is frequently seen with impairment of the heart muscle or the coronary system When the rise of venous pressure is acute and sharp it can act upon receptors in the auricles and in the large veins causing an acceleration of the heart rate through the cardiac sympathetic nerves This is the Bainbridge reflex The reverse of this, a depression in venous pressure responsible for a slowing of the cardiac rate, is not established A reflex described by McDowall and supposed to start in the right auricle is due to an increase in venous pressure The reflex produces stimulation of the sympathetic innervations leading to vasomotor constriction with an increase in systemic blood pressure

(h) *Peripheral Vascular Phenomena* These occur mainly as intermittent claudication of the lower limbs, but claudication can also affect the upper extremities the vessels of the fundi oculi the brain and in the thorax and abdomen Many years ago, Pal[30-31] called attention to vascular spasms or crises as *he termed them and a form of intermittent claudication which attacks the* pulmonary vessels has been described by Posselt[38] manifested by tightness and general distress in the chest All these spastic phenomena probably depend upon sympathetic vasoconstriction

The mechanism of the spasm which seizes the coronary vessels has received a good deal of study especially in animals under experimental conditions (Manning et al,[1] McEachern et al[23] Opdyke and Selkurt[9]) and it is generally agreed that the impulses travel by vagal pathways The clinical aspect of reflex vasoconstriction will therefore be discussed under the parasympathetic effects (p 37)

2 *Shock*

Although the action of the autonomic nervous system in shock seems to be chiefly depressor in character, pressor effects account for the constriction of the splanchnic vessels the cutaneous vascular bed and of arterioles in other parts of the body The depressor manifestations are prominent (p 35)

3 *Respiratory Features*

The pulmonary vessels may become constricted as a result of regional (pulmonary) or generalized sympathetic autonomic discharge This is observed in angina pectoris or acute myocardial infarction or it may persist after the acute attack Changes in respiratory rate and rhythm are often due to central effects occurring either as primary responses on the part of the respiratory autonomic representations in the brain stem and cortex or as reactions brought on by the influence of metabolites or excessive edema fluid acting on the respiratory centers Dissociation of the integrated pattern of respiration takes place only when the cerebral zones of respiratory regulation are severely compromised [76]

The respiratory manifestations can also follow stimulation of the sympathetic fibers which innervate the bronchial musculature and relax it As a matter of interest the administration of epinephrine in asthma or other acute paroxysmal states relaxes the bronchial musculature in this way it acts by relaxing the bronchial musculature through sympathetic stimulation the cautious use of epinephrine may be advisable to bring about this relief even in the presence of anginal pain (p 281)

4 *Gastrointestinal Features*

The sympathetic motor nerves of the gastro-intestinal musculature consist of a group of efferent fibers which leave the neuraxis between Th 6 and L 4 inclusive forming the splanchnic nerves They innervate not only the musculature glandular elements but also blood vessels of the alimentary tract Sympathetic stimulation can therefore cause constriction of the vascular supplies of this tract

The sympathetic nerves inhibit contraction of the gastro-intestinal musculature This inhibitory effect can lead to acute gastric *dilatation* atony of the bowels meteorism and flatulence and belching are probably associated phenomena The symptoms may arise prior to an attack of acute myocardial infarction or acute coronary insufficiency or they *may* precipitate the attack Attacks of this nature have been labeled in the past as indigestion or ptomaine poisoning but they are in reality cardiac episodes and dangerous Not only flatulence and belching but hyperchlorhydria and cardialgia *may* precede or accompany an acute cardiac episode or persist long after *the* attack The gastro-intestinal events which precede an attack have been studied extensively by Verdon [81] Compared to circulatory features *the* gastro-intestinal manifestations are of secondary import but they may take *on major* significance and throw the balance from recovery to no recovery *especially* if the heart has been badly damaged Meteorism can be a great offender in this respect and vomiting too

5 *Sudomotor Reaction (Sweating)*

Pallor flushes, clamminess of many parts of the surface of the body are quite common during and shortly after an acute attack of acute coronary insufficiency free of or complicated by acute myocardial infarction The clamminess is due to sweating associated with vasoconstriction of the skin vessels Sweating may be drenching and aggravate the fatigue and asthenia which soon follow the attack The sweating often is manifested through the fiber paths which transmit anginal pain and thus remain limited to the dermatomes innervated by the left thoracic segments 1 to 4, or the sweating can take a patchy or bizarre pattern on the body surface or it may be generalized and independent of pyrexia, excessive in the day time or at night, and unrelated to the mobility or physical activity of the patient After an attack of acute myocardial infarction sweating may persist for weeks lingering as a sole symptom when all other evidences of the attack have apparently subsided Sweating of this order is a serious symptom and speaks for a generalized disturbance of the autonomic apparatus not yet come to rest Very occasionally sweating as well as flushes pallor, paresthesias yawning, or insomnia may be a forerunner of an oncoming attack The restriction of fluid or sodium chloride or the administration of atropine have little influence on this sweating Sweating is grouped with sympathetic manifestations because it is induced by central autonomic representations throughout the neuraxis The peripheral limb of the pathway is, however parasympathetic and this explains the blocking effect sometimes obtained by atropine

6 *Pilomotor Reactions*

Erection of the body hair a striking feature in lower forms is not prominent in the human subject Nevertheless these manifestations can occur in man and represent a sympathetic effect of the pilomotor apparatus The reaction in colloquial parlance is known as goose pimples or goose flesh Pilomotor activities have been produced experimentally in cats for example by stimulating the posterior hypothalamus (Case E K developed during an attack of angina pectoris, generalized sudomotor and pilomotor changes whereas the skin of the upper half of the body was warm and red and the skin of the lower half was grey, cold and clammy See p 58)

B THE PARASYMPATHETIC MANIFESTATIONS

Parasympathetic manifestations are generally prone to be less regional namely more wide spread and generalized than in the case of sympathetic manifestations but this is not a fast rule

1 *Shock*

This condition is not a usual accompaniment of mild or moderate acute coronary insufficiency It may, however appear in a protracted unrelieved

attack and is more frequent and pronounced when acute myocardial infarction occurs The degree of shock is variable In severe shock the circulatory manifestations are marked and to the fore venous pressure is lowered cardiac output reduced peripheral circulation slowed the splanchnic area overfilled with blood and the cutaneous vascular bed constricted Cutaneous pallor peripheral collapse and cardiac failure are the clinical features of shock These reactions are for the most part depressor in character and stem chiefly from activities in the brain stem Sympathetic vasoconstriction however can eventually get the upper hand or become manifest even during the state of shock This can be evidenced by constriction of arteriolar beds in various parts of the body especially the splanchnic region and the skin

2 *Exhaustion and Prostration*

Prostration or a sense of exhaustion is often a sequel to a paroxysm (attack) of acute coronary insufficiency Even a mild attack can bring this on with variations from listlessness lassitude to a deep weariness or leaden heavy tiredness or prostration Prostration or exhaustion may antecede the attack or persist for some time usually it is not long lived Exhaustion and prostration in severer and more protracted forms are apt to appear with acute myocardial damage with or without acute coronary occlusion Since the adrenal sympathetic upheaval primarily an emergency reaction is characterized by vigor and hyperactivity not by lassitude and fatigue it may therefore be inferred that prostration and fatigue are parasympathetic effects However one cannot be too dogmatic on this point

3 *Cardiovascular Features*

The action of the heart may remain surprisingly good not perceptibly deranged or altered and the rate unchanged or moderately slowed the cardiac output normal Indeed cardiac disturbances during an attack of acute coronary insufficiency (angina pectoris) and even in rare cases of acute myocardial infarction with or without acute coronary occlusion may be minimal almost absent The parasympathetic system appears to keep the heart and the gastrointestinal tract in line to hold these organs fast during the autonomic upheaval which accompanies the acute onslaught on the cardiac apparatus It is accordingly not too surprising that bradycardia occasionally develops and its appearance has been interpreted clinically as a favorable sign in acute cardiac infarction

Depressor manifestations may be very pronounced in acute myocardial infarction associated with coronary thrombosis of a major vessel Severe collapse may quickly follow the initial infarction When the heart has to combat the superadded effect of fresh or advancing myocardial damage before collateral coronary circulation has had an opportunity to bring aid to the heart the depressor effects may become irreversible and death imminent The excessive

(depressor) effect on the circulation, manifested by very low blood pressure and other features of circulatory collapse, is too great a disability for the maimed heart and crippled coronary system to overcome But there are instances as severe as this when, despite circulatory depression, the heart can make the grade if not mortally injured

The arterial blood pressure is little if at all disturbed in uncomplicated acute coronary insufficiency but it will decline sharply, as a rule from a previous normal or hypertensive level following acute myocardial infarction The systolic and diastolic pressures fall, the former markedly, and the pulse pressure is reduced The prognosis becomes grave as the drop in blood pressure stays unrelieved for days or even hours, a systolic pressure of less than 70 mm Hg has an extremely grave import (Mintz and Katz [7]) Diastolic pressure held at a low level is also an extremely unfavorable sign The hypertensive individuals will exhibit a greater fall in blood pressure than patients with normal levels, but in them a hypotension below 100 mm Hg which endures several days carries a very serious outlook Eventually, if the patient lives for one or two years after the attack, the blood pressure is very likely to return to its previous level and this seems to be true for patients with normal or hypertensive levels The depressor effect on blood pressure can however, persist for months and even years, indicating that the hypotension from the beginning or at any rate after the subsidence of the attack, is not cardiogenic, i e , produced by a diminished cardiac output associated with forward failure

A *first episode of angina pectoris or of acute myocardial infarction* with acute coronary occlusion, even in victims who have been free of hypertensive cardiovascular disease can result in an early death, congestive heart failure having no opportunity to develop An acute coronary occlusion it is claimed by Gilbert and his co workers [8, 9] can set up reflex vagal constriction of un occluded coronary vessels The reflex is vagal, unless one agrees with Katz and Jochim[16] that the constriction of the coronary vessels is by sympathetic nerves Constriction of the coronary vessels may lead to fresh or increased anginal pain and to other deleterious effects on the cardiovascular apparatus The depressor effects on the circulation include the special activities of the carotid and aortic sinuses and the influence of the vagal innervations on the hepatic veins The hepatic vein barriers ' Venensperre (p 95) have been shown to exercise a regulatory effect on water regulation of the body but their role in congestive heart failure is not known

During the acute attack or very shortly thereafter the heart action may become weak and *the sounds take on a muscular muffled quality* and the rhythm, fundamentally sinus may become intercepted by single or by groups of extrasystoles True pulsus alternans is not an accompaniment of angina pectoris, but is encountered in advanced long standing hypertension and in patients whose hearts have been weakened by *repeated onslaughts of myocardial infarction* The heart may stop in standstill or ventricular fibrillation This

latter event in a manner of speaking is the way in which the heart signs off before it stops Schwartz[43] has however described patients with myocardial damage and coronary occlusion who survived numerous attacks day after day

Reflex Coronary Constriction It is claimed that in the dog acute infarction of the myocardium experimentally produced will give rise to stimuli which cause reflex coronary vasoconstriction and that the pathway of such a reflex is by afferent sensory fibers from the heart and by efferent vagal fibers to the coronary system (LeRoy and Snider[17]) Nervous impulses from the primary ischemic area of the heart caused by acute coronary occlusion are said to induce a temporary reflex spasm of other coronary arteries resulting in secondary ischemic areas Furthermore the reflex coronary constriction can lead to fatal ventricular fibrillation (LeRoy and Snider[17]) the reflex is abolished by anesthesia (Manning et al[20]) and xanthine derivatives and atropine help to reduce the secondary ischemic areas (LeRoy et al[18]) The effect of anesthesia and drugs such as papaverine in this connection has recently been investigated again by Opdyke and Selkurt[24]

According to Greene[12, 13] and Gilbert et al[8, 9] an acute cardiac infarction in man as well as in the dog can produce a similar train of events Reflex vagal coronary constriction is an accompanying danger and the constriction may cause ventricular fibrillation and sudden death or the manifestation only of anginal pain

4 *Respiratory Changes*

The pulmonary arterial bed after initial sympathetic constriction may undergo parasympathetic dilatation Generally speaking the pulmonary apparatus has to overcome two strong influences sympathetic constriction of its vascular bed and parasympathetic constriction *of the bronchial* musculature A depressor effect already alluded to is *observed in the* vagal slowing of the cardiac rate This is often considered a *favorable sign* in the presence of severe myocardial damage The heart is retarded *because the* pacemaker of the heart is slowed and not because as in heart block *for instance* the junctional tissues have been affected

(a) *Apnea* True apnea must be distinguished from voluntary braking of the respiration as witnessed in a patient *for* example who strives to remain immobile during the excruciating *agony of the* attack breathing is here deliberately avoided or kept shallow Osler[2, 31] has described in this connection holding the breath as long as possible An attack of angina pectoris seldom accelerates or diminishes ventilation *Although* apnea is not unknown when the heart is severely damaged it is unlikely in uncomplicated *acute* coronary insufficiency

(b) *Dyspnea* Shortness of breath true dyspnea is not foreign to the picture It can be produced by a coronary *system* incompetent to bring the quantity of oxygen needed by the heart to enable this organ *to* deliver adequate blood

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to the respiratory centers, and the dyspnea can be aggravated by parasympathetic constriction of the bronchial musculature, producing asthma like paroxysms

Noncardiac dyspnea is not to be mistaken for the dyspnea just described The former, an added and troublesome affliction during a cardiac attack has a paroxysmal character of its own and is irregular in occurrence It is associated with bronchial edema, emphysema, bronchiectasis or other pulmonary disorders or is caused by some antecedent cardiovascular disease not related to the acute cardiac episode Heberden[14] claimed there is "no shortness of breath" in a cardiac attack, but he was mistaken Libman[0] believed that dyspnea "covers" pain in hypersensitive subjects with angina pectoris and he meant by this that dyspnea could be a substitute or the equivalent of pain and that the dyspnea submerges or suppresses pain Cheyne Stokes breathing is a tell tale of cerebral respiratory disturbance and an alarming complication but need not be a portent of an immediate fatal outcome The Biot type of breathing is seldom seen

(c) *Hemoptyses* To evaluate the specific influence of the parasympathetic or sympathetic division in relation to pulmonary hemoptyses is not simple The parasympathetic supplies dilate the pulmonary vascular bed and so increase the pulmonary reservoir, but this does not mean that the parasympathetic innervations to the lungs are necessarily overactive in connection with hemoptysis Hemorrhage from the lung is produced as a rule by thrombi which lodge in the pulmonary circulation These thrombi are prone to form in the presence of fresh myocardial infarction especially if acute coronary occlusion has occurred, involving the septum or fairly large areas of the walls of the heart Thrombi formed in the right heart are readily ejected into the lungs to produce pulmonary thrombi but thrombi which arise in varicose leg veins in the prostatic plexus or at other extracardiac sites can also cause pulmonary infarction and hemoptyses

Pain associated with pulmonary embolus and hemoptyses is not infrequent The pain may be intense involving the chest in general or it may be restricted to the left side or remain midsternal as in precordial anginal pain Indeed, pulmonary embolization with hemoptysis may ape or even masquerade as an acute myocardial infarction, or both conditions may co exist Atypical forms of pericarditis may simulate an attack of acute coronary occlusion or even pulmonary embolization, when frank bleeding from the lungs is absent The electrocardiographic picture usually distinct and almost specific in acute coronary occlusion with infarction of the posterior wall may have common and confusing features in acute pulmonary embolization and in acute pericarditis

5 *Gastro intestinal Features*

The parasympathetic supplies to the gastro intestinal tract increase the tone of the alimentary musculature Accordingly, autonomic effects would be

registered as increased peristalsis with diarrhea or colic (spasm) Constriction of the epigastric muscles or of the esophageal and pharyngeal structures has been attributed to parasympathetic effects associated with general autonomic reaction set off by an anginal seizure

BIBLIOGRAPHY

ALLBUTT T C Diseases of the arteries including angina pectoris London Macmillan 1915

AVERBUCK S H Acute generalized postoperative peritonitis simulating coronary artery thrombosis J Mt Sinai Hosp 1942 8 33

BING R L VAN DAM L D GREGOIRE F HANDELSMAN J C GOODALE W T AND ECKENHOFF J E Catheterization of the coronary sinus in man Proc Soc Exper Biol & Med 1947 66 239

BLUMGART H L SCHLESINGER M J AND DAVIS D Studies on the relation of the clinical manifestations of angina pectoris coronary thrombosis and myocardial infarction to the pathologic findings Am Heart J 1940 19 1

— AND ZOLL P Angina pectoris coronary failure and acute myocardial infarction The role of coronary occlusion and collateral circulation J A M A 1941 116 91

COURNAND A Measurement of the cardiac output in man using the right heart catheterization Fed Proc 1945 4 207

DANIELOPOLU D L angine de poitrine et l angine abdominale Paris Masson 1927

GILBERT N C FENN G K AND LEROY G V The effect of distention of abdominal viscera on the coronary blood flow J A M A 1940 115 1962

— LEROY G V AND FENN G K The effect of distention of abdominal viscera on the blood flow of the circumflex branch of the left coronary artery of the dog Am Heart J 1940 20 519

GOODALE W T LUBIN M ECKENHOFF J E HAFKENSCHIEL J H AND BANFIELD W G JR Coronary sinus catheterization for studying coronary blood flow and myocardial metabolism Am J Physiol 1948 152 340

— — — — DURLACHER S H LANDING B H AND BANFIELD W G Coronary sinus catheterization technique for studying coronary blood flow and myocardial metabolism in vivo Proc Soc Exper Biol & Med 1947 66 571

GREENE C W The nervous control of the coronary vessels with new experimental evidence for the pathways of efferent constrictor and dilator neurones in the dog Am J Physiol 1935 113 361

— Control of the coronary blood flow by reflexes arising in widely distributed regions of the body Am J Physiol 1935 113 399

HEBERDEN W Some account of a disorder of the breast Med Tr Coll Phys London 1772 2 59

HICKAM J B AND CARGILL W H Effect of exercise on cardiac output and pulmonary arterial pressure in normal persons and in patients with cardiovascular disease and pulmonary emphysema J Clin Investigation 1948 27 10

KATZ L N AND JOCHIM K Observations on the innervation of the coronary vessels of the dog Am J Physiol 1939 126 395

LEROY G V AND SNIDER S S The sudden death of patients with few symptoms of heart disease J A M A 1941 117 2019

— FENN G K AND GILBERT N C The influence of xanthine drugs and atropine in the mortality rate after experimental occlusion of a coronary artery Am Heart J 1942 23 637

LIAN C La angine de poitrine Paris Masson 1932

20 LIBMAN, E Observations on individual sensitiveness to pain J A M A 1934 *10?* 335
21 MANNING G W, MCEACHERN C G AND HALL G E Reflex coronary artery spasm following sudden occlusion of other coronary branches Arch Int Med 1939 *64* 661
22 MCDOWALL R J S A vagopressor reflex J Physiol 1929 *59* 41
23 MCEACHERN C G MANNING G W AND HALL G E Effects of sudden occlusion of coronary arteries following removal of cardiosensory pathways Arch Int Med 1940 *65* 661
24 MCMICHAEL J AND SHARPEY SCHAEFER E P Cardiac output in man by a direct Fick method Brit Heart J 1944 *6* 33
25 MERRILL A J *Edema and decreased renal blood flow in patients with chronic congestive* heart failure evidence of forward failure as the primary cause of edema J Clin Investigation 1946 *25* 389
26 MILLER H R Central Autonomic Regulations in Health and Disease New York Grune & Stratton 1942
27 MINTZ S S AND KATZ L N Recent myocardial infarction an analysis of five hundred and seventy two cases Arch Int Med 1947 *80* 205
28 OPDYKE D F AND SELKURT E E A study of alleged intercoronary reflexe following coronary occlusion Am Heart J 1948 *36* 73
29 OSLER, W Lectures on Angina Pectoris and Allied States New York D Appleton & Co 1897
30 —— Angina pectoris as an early symptom in aneurysm of the aorta Med Chron 1906 *11* 69
31 —— Lumleian lecture Lancet 1910 *1* 697
32 PAL J Über die Innervation der Leber Med Jahrb 1888 *3* 67
33 —— Gefasskrisen Leipzig Hirzel 1905
34 —— Die Tonuskrankheiten des Herzens und der Gefasse ihre Biologie und Therapie Wien J Springer 1934
35 PARIN V V The role of pulmonary vessels in the control of the blood circulation Am J M Sc 1947 *214* 167
36 POSSELT A Die klinische Diagnose der Pulmonalarteriensklerose Munchen m l Wchnschr 1908 *55* 1625
37 PRINZMETAL M SIMKIN B BERGMAN H C AND KRUGER H E Studies on the coronary circulation II The collateral circulation of the normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres Am Heart J 1947 *33* 420
38 —— BERGMAN H C KRUGER H E SCHWARTZ L SIMKIN B AND SOBIN S S Studies on the coronary circulation III Collateral circulation of beating human and dog hearts with coronary occlusion Am Heart J 1948 *35* 689
39 RANDLES I S HIMWICH W A HOMBURGER E AND HIMWICH H E The influence of vitamin B_1 deficiency on the pyruvate exchange of the heart Am Heart J 1947 *33* 341
40 SAHLI H Verhand d Kongr f inn Med 1901 *19* 45
41 SCHERF D AND SCHONBRUNNER E Über Herzbefunde bei Lungenembolien Ztschr f klin Med 1935 *128* 455
42 —— and —— Über den pulmokoronaren Reflex bei Lungenembolien Klin Wchnschr 1937 *16* 340
43 SCHWARTZ S P Transient ventricular fibrillation A study of the electrocardiograms obtained from a patient with A V dissociation Recurrent syncopal attacks Arch Int Med 1932 *50* 450
44 SPIEGEL E A Über das Wesen des Bauchschmerzes und seine Begleiterscheinungen Wien med Wchnschr 1927 *77* 379
45 —— Experimentelle Neurologie Berlin S Karger 1928
46 —— Visceral and vascular pain Proc Soc Staff Meet Mayo Clin 1930 *5* 213

[7] STEAD E A JR WARREN J V AND BRANNON E S Cardiac output in congestive heart failure Am Heart J 1948 35 529

[8] STRUEFF N Zur Frage der bakteriellen Lungenembolie, Virchow s Arch 1909 195 211

[9] TROUSSEAU A Clinique medicale de l Hôtel Dieu de Paris 5th edition Paris J B Baillière et fil 18 7

[10] VAQUEZ H Diseases of the Heart Translated by G F Laidlaw London and Philadelphia W B Saunders Co 1924

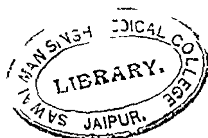
[11] VERDON W Angina Pectoris Brighton England W T Moulton & Co 1920

[12] VILLARET M JUSTIN BESANÇON L AND BARDIN P Physio-pathologie des accidents mortels consécutifs aux embolies pulmonaires Bull et mém Soc Méd d hôp de Paris 1936 52 936

[13] —— —— AND —— Recherches sur la prévention expérimentale des accidents consécutifs aux embolies pulmonaires Bull et mém Soc méd d hôp de Paris 1936 52 941

[14] WARREN J V AND STEAD E A JR Fluid dynamics in chronic congestive heart failure Arch Int Med 1944 73 138

[15] YANOF Z A Blood pyruvic acid in heart disease Arch Int Med 1942 69 1005



[20] LIBMAN, E Observations on individual sensitiveness to pain J A M A 1934 *102* 335

[21] MANNING G W McLACHERN C G, AND HALL G E Reflex coronary artery spasm following sudden occlusion of other coronary branches Arch Int Med 1939 *64* 661

[22] McDOWALL R J S A vagopressor reflex J Physiol 1929 *59* 41

[23] McEACHERN C G MANNING G W AND HALL G E Effects of sudden occlusion of coronary arteries following removal of cardiosensory pathways Arch Int Med 1940 *65* 661

[24] McMICHAEL J, AND SHARPEY SCHAFER, E P Cardiac output in man by a direct Fick method Brit Heart J 1944 *6* 33

[25] MERRILL A J *Edema and decreased renal blood flow in patients with chronic congestive* heart failure evidence of forward failure as the primary cause of edema J Clin Investigation 1946 *25* 389

[26] MILLER H R *Central Autonomic Regulations in Health and Disease* New York Grune & Stratton 1942

[27] MINTZ S S AND KATZ L N Recent myocardial infarction an analysis of five hundred and seventy two cases *Arch Int Med* 1947 *80* 205

[28] OPDYKE D F AND SELKURT E E A study of alleged intercoronary reflexes following coronary occlusion Am Heart J 1948 *36* 73

[29] OSLER, W Lectures on Angina Pectoris and Allied States New York D Appleton & Co 1897

[30] —— Angina pectoris as an early symptom in aneurysm of the aorta Med Chron 1906 *11* 69

[31] —— Lumleian lecture Lancet 1910 *1* 697

[32] PAL J Über die Innervation der Leber Med Jahrb 1888 *3* 67

[33] —— Gefässkrisen Leipzig Hirzel 1905

[34] —— Die Tonuskrankheiten des Herzens und der Gefässe ihre Biologie und Therapie Wien J Springer 1934

[35] PARIN V V The role of pulmonary vessels in the control of the blood circulation Am J M Sc 1947 *214* 167

[36] POSSELT A Die klinische Diagnose der Pulmonalarteriensklerose Munchen med Wchnschr 1908 *55* 1625

[37] PRINZMETAL M SIMKIN B BERGMAN H C AND KRUGER H L Studies on the coronary circulation II The collateral circulation of the normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres Am Heart J 1947 *33* 420

[38] —— BERGMAN H C KRUGER H E SCHWARTZ L SIMKIN B AND SOBIN S S Studies on the coronary circulation III Collateral circulation of beating human and dog hearts with coronary occlusion Am Heart J 1948 *35* 689

[39] RANDLES F S HIMWICH W A HOMBURGER E AND HIMWICH H E The influence of vitamin B_1 deficiency on the pyruvate exchange of the heart Am Heart J 1947 *33* 341

[40] SAHLI H Verhand d Kongr f inn Med 1901 *19* 45

[41] SCHERF D AND SCHONBRUNNER E Über Herzbefunde bei Lungenembolien Ztschr f klin Med 1935 *128* 455

[42] —— and —— Über den pulmokoronaren Reflex bei Lungenembolien Klin Wchnschr 1937 *16* 340

[43] SCHWARTZ S P Transient ventricular fibrillation A study of the electrocardiograms obtained from a patient with A V dissociation recurrent syncopal attacks Arch Int Med 1932 *50* 450

[44] STIEFEL L A Über das Wesen des Bauchschmerzes und seine Begleiterscheinungen Wien med Wchnschr *1927 77 379*

[45] —— Experimentelle Neurologie Berlin S Karger 1928

[46] —— Visceral and vascular pain Proc Soc Staff Meet Mayo Clin 1930 *5* 213

the possible development of the insufficiency in the absence of pre existing or simultaneous injury to the heart or coronary vessels It is claimed that young marathon runners taxed to the breaking point may develop acute coronary insufficiency as a forerunner of acute cardiac dilatation but it is still a controversial matter whether excessive physical or emotional strain as commonly observed in routine living or work is a competent producing cause in young people possessing a sound unimpaired cardiovascular apparatus The electrocardiographic records which follow have been selected with these problems in mind

1 *Acute Coronary Insufficiency in Subjects with Normal or Ostensibly Normal Cardiovascular Apparatus*

The following cases of acute coronary insufficiency occurred in individuals in whom pre existing cardiovascular disease was excluded with reasonable certainty

Bleeding from Peptic Ulcer

A young man of 33 I D developed an acute attack of coronary insufficiency following a loss of blood from a bleeding peptic ulcer the hemoglobin dropped to 41 per cent

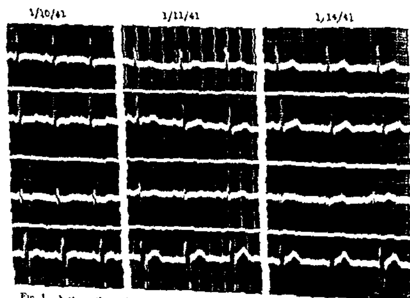


Fig 1 *Note in the first tracing* a mild depression of RST in leads I and II and a reduction of the voltage and inversion of T in all leads The RST *depression disappeared* the next d and *the T* waves began to be upright (second tracing) Three days *later the T* waves were practically of normal voltage The ventricular rate was not increased (third tracing) This case demonstrates that changes *in T* waves may be the predominant feature

CHAPTER III

Electrocardiographic Findings in Angina Pectoris, Acute Myocardial Infarction and Acute Extracardiac Conditions

Excellent text books and reference sources are available for those interested in electrocardiography or the more highly specialized aspects of electrophysiology. The discussion in this chapter will therefore be limited to the *findings which go with the cardiac and related conditions considered in this volume.*

I. Acute Cardiac Conditions

A. *Acute Coronary Insufficiency*

The ST (or RST) segment is sharply depressed* in one or more standard limb leads and in precordial leads; an abnormal depression in one limb lead is often sufficient for the diagnosis. The T wave need undergo no change or it may be flattened or inverted. Q waves are absent. T wave changes alone, i.e., in the absence of RST changes, are sufficient for the diagnosis. There are times when the diagnosis is reached only after several tracings.

Similar changes in RST and T are produced by digitalis. The RST depression in acute coronary insufficiency in the absence of myocardial involvement comes on abruptly with the onset of coronary derangement and disappears abruptly when the coronary circulation is righted, whereas the RST deformed by digitalis is restored more slowly, taking days or weeks after the drug is stopped. *The effect of digitalis may be visible after an acute episode of coronary insufficiency is over, indicating that the electrocardiographic changes were independent of the coronary insufficiency.* Frequently, however, it is not possible to determine whether the electrocardiographic signs are due to digitalis or to *acute coronary insufficiency or to other factors.*

Excepting cases induced by acute exsanguination or acute CO poisoning or other severe disabling causes from which even normal coronary vessels and heart muscle would not be expected to escape damage, acute coronary insufficiency is rare in young healthy individuals. A practical point for them concerns

* The amount of ST shift which constitutes "abnormal" is not agreed upon by all authorities. According to Katz[7] it consists of an elevation of more than 2 mm. in the limb leads and in CF2, CF4 and CF5 or a depression of 0.5 mm. in leads I and II, 1.0 mm. in lead III, or any degree in CF2 and CF4, or any amount greater than 0.5 mm. in CF5. Burch and Winsor[1] feel that a shift of 1 mm. above or below the isoelectric line in the standard leads is abnormal.

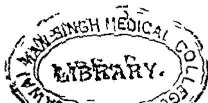
Response to Nicotine

A normal 24 year old woman D P who had limited herself to two cigarettes a week because smoking caused palpitations and heartburn received 2 mg of nicotine bitartrate intravenously

A B C

I II III IVF

Fig 2 — A control with the needle in the vein The heart rate was 88 and the blood pressure 110/65 B one minute after injection she became dizzy and faint the heart rate was 136 and the blood pressure 130/85 The tracing shows tachycardia reduced voltage of the T waves in all leads and depression of the RST segment in leads I II and III C nine minutes after injection heart rate was 98 and blood pressure 115/65 (From Am Heart J 1947 34 65)



Acute Hypoxia with Marked Anemia

A young male, aged 22, with chronic anemia, chronic persistent hook worm infestation, and marked secondary anemia (Hgb 6 Gm per 100 cc blood)

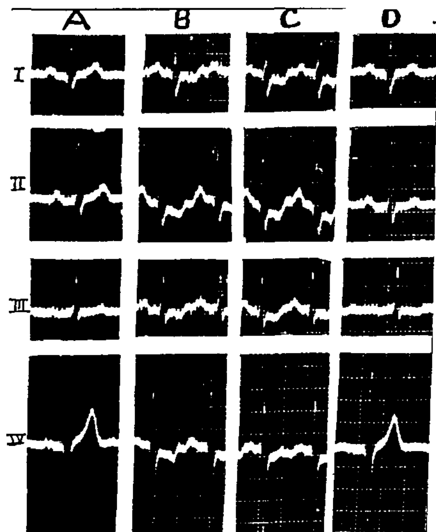


Fig 1a —Tracing A is the control and is normal indicating that the anemia had produced no coronary insufficiency B is the tracing after ten minutes exposure to 10 per cent O_2 Marked depression of RST in all leads the T wave is inverted in leads I II III and IV C is the record after twenty minutes exposure to 10 per cent O_2 and shows practically the same findings as B D shows the recovery after breathing 100 per cent oxygen and then room air (From Ann Int Med 1947 *26* ,41)

Post-operative Shock

A 59 year old male M C developed acute coronary insufficiency with the onset of post-operative shock Although he was not known to have pre-existing cardiovascular disease the possibility of its presence can not be excluded

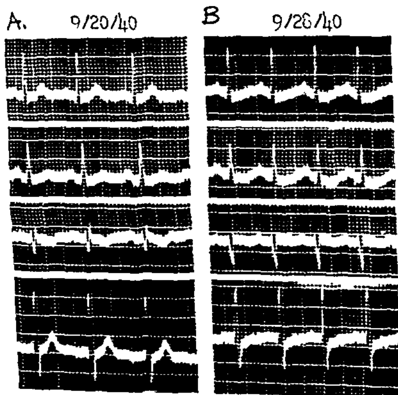


Fig 6—Tracing B shows depression of RST and inversion of the T wave in leads I II and IV The ventricular rate is increased

Undue Exertion

A woman of 52, E W, with hypertensive cardiovascular disease (coronary sclerosis) and diabetes mellitus, developed an acute attack of coronary insufficiency while undergoing the Master two step exercise test

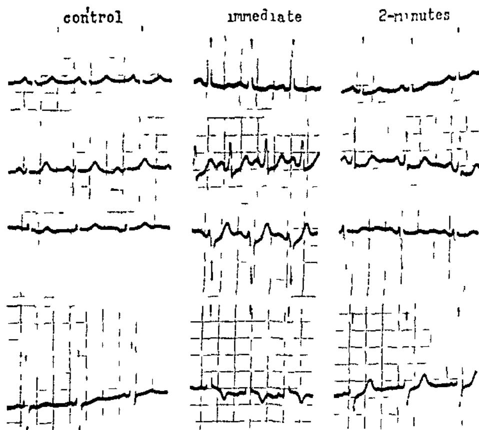


FIG 5—Immediately after exertion RST became depressed in leads II and III T wave inversion appeared only in leads I and IV

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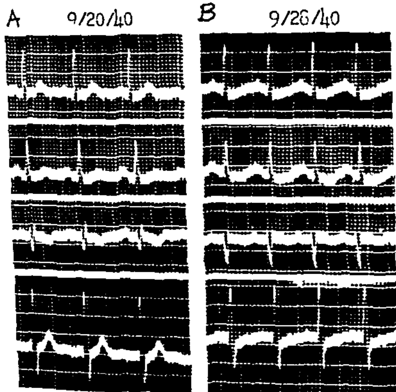


Fig 6—Tracing B shows depression of RST and inversion of the T wave in leads I II and IV The ventricular rate is increased

Response to Nicotine

G M a man 50 years old, a moderate smoker, with antecedent coronary and anginal pain, received 2 mg of nicotine bitartrate intravenously

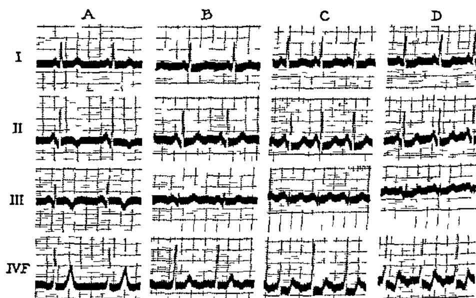


Fig 7 — A Two weeks after cardiac infarction Nicotine study made three months later B Control needle in vein Rate 90 blood pressure 140/80 C Two minutes after injection Rate 120 blood pressure 144/86 Record shows acute coronary insufficiency depression of RST segment in leads I II and IV and partial inversion of the T wave in the precordial lead D Fifteen minutes after injection Rate 102 blood pressure 148/82 No anginal pain but complained of dizziness and tingling The record shows little change from C (From Am Heart J 1947 *34* 65)

Undue Emotions

A 36 year old male R J R, who had experienced previous anginal mani tations associated with hypertension and coronary sclerosis developed ute coronary insufficiency and acute myocardial damage brought on by ief over the death of his father He succumbed seven weeks later The autopsy vealed severe coronary sclerosis but not complete occlusion the left ventricle is severely infarcted but the pericardium and endocardium were intact

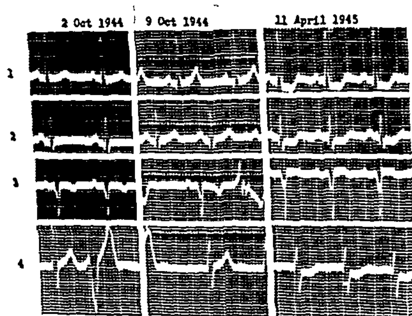


Fig 8—The electrocardiogram of October 2 1944 reveals myocardial involvement that of October 9 1944 restitution to practically normal state the last record April 11 1945 shows acute coronary insufficiency RST depressions and semi inversion of T waves in leads I II and IV The precipitating element in the attack occurred seven weeks before he expired on April 12 1945

These electrocardiographic records depict a general agreement with the physiologic pathologic and clinical state in each case but striking exceptions occur. An acute violent attack of coronary insufficiency in the absence of corroborative electrocardiographic signs was a striking aspect in the following case.

The patient A B aged 48 after a very heavy large meal late at night developed within a very short time collapse with intense precordial pain radiating into the arm and shoulder a fall in blood pressure from normal level 128/88 to 80/50 breathlessness and imperceptible pulse. The condition was diagnosed by trained observers as acute coronary insufficiency. The acute episode was over within a few hours the blood pressure began to rise and was restored to normal within a day. The electrocardiogram was negative shortly after the attack four days later and after ten days.

A similar discrepancy was exemplified in a case of rheumatic heart disease.

A young woman A O incapacitated with rheumatic heart disease since the age of 8 was admitted to Montefiore Hospital at the age of 32. She had ten to twenty attacks of typical incapacitating anginal pain every twenty four hours during a long period of observation. The electrocardiogram during and between anginal attacks revealed no acute coronary insufficiency. There was however little doubt that the coronary circulation had been responsible for the repeated paroxysms of anginal pain the attacks were completely arrested by aminophyllin.

B Acute Myocardial Infarction without Acute Coronary Occlusion

The electrocardiographic signs are sometimes indistinguishable from those of acute coronary insufficiency. As a rule, however, the findings last longer, the prominence and persistence of the RST depression and T wave inversion depend upon the extent and duration of the subendocardial damage. Elevation of the ST segment is rare but occurs if the epicardial layer of the heart is involved. Eventual recovery from the myocardial damage is usually accompanied by restoration of the electrocardiogram to a normal or almost normal state. Q waves are nearly always absent.

The electrocardiogram in about 5 per cent of cases of acute myocardial *infarction unattended by coronary occlusion may show signs* which are char*acteristic of acute myocardial infarction associated with acute coronary* occlusion. This occurs when the myocardial lesion is no longer subendothelial but involves the endothelial as well as the epicardial layers of the heart. The lesion thus is in effect a massive through and through infarction and the associated electrocardiographic signs may then point to predominantly anterior or posterior wall involvement (Fig 9).

C Acute Myocardial Infarction with Acute Coronary Occlusion

Whereas in the type of acute myocardial infarction described above the lesion consists of scattered multiple focal necroses which comparatively seldom penetrate the endothelial lining of the heart, in acute myocardial infarction

Acute Myocardial Infarction without Coronary Occlusion

Acute myocardial infarction induced by severe emotional stress A 46-year old male M C with hypertension of less than one year s duration (190 120) and polycythemia (Hgb 105 per cent), suddenly developed after an intense emotional altercation severe precordial pain, circulatory collapse profuse sweating and prostration

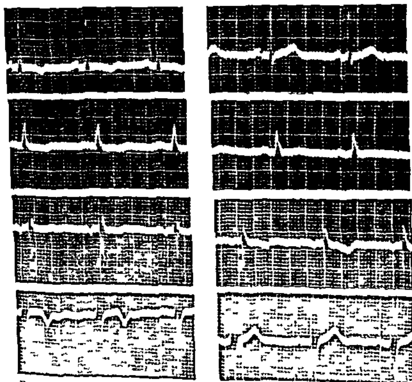


FIG 9—Note the acute inversion of T waves in leads I II and IV in the record of 30-46 (left) This came on with the sudden collapse and was gone by 9-4-46 (right)

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Anterior Wall Infarction with Acute Coronary Insufficiency

J J a man of 68 with generalized arteriosclerosis associated with moderate hypertension of several years standing developed an acute seizure of intense precordial pain radiating into the left arm this was accompanied by general collapse fever and leukocytosis

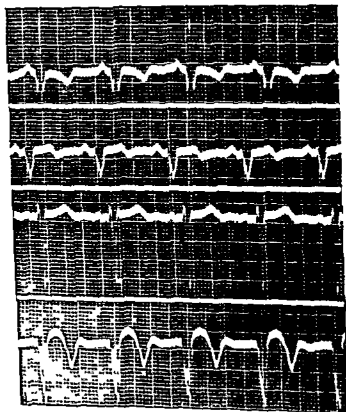


Fig 10a — Note the elevation of the RST segment in leads II III and IV T is inverted and cove shaped in lead I and IV and inverted in lead II Deep Q waves appear in leads I and IV

with coronary occlusion the lesion is practically always homogeneous massive and includes the inner and outer layers of the heart wall The electrocardiographic signs differ as a rule with respect to localization of the myocardial lesion in the anterior or posterior wall

When the anterior wall of the heart is damaged, the RST segment in leads I and IV* is elevated and shows a high take off The high take off is due to pericardial involvement (Scherf and Boyd[9]) The T waves in leads I and IV are inverted and soon assume a typical cove shape, Q waves are prominent in leads I and IV The findings in leads I and III are often reciprocal The precordial leads derived from the chest wall over the area of infarction disclose elevated RST segments and inverted T waves The T waves in the precordial and limb leads may gradually become righted or remain inverted and smaller as permanent evidence of infarction, in some cases the IV lead will show an inverted or upright T of high voltage long after the acute episode of infarction The RST changes in the standard an precordial leads tend eventually to reach the isoelectric line, but some degree of shift of the segment may persist or even remain permanent (Fig 10a)

When the posterior wall of the heart is infarcted the RST segment is elevated in leads II and III, the T waves are inverted and become cove shaped and Q waves appear in leads II and III Similar changes are noted in the precordial leads derived from the chest wall over the area of infarction The RST segment in all leads tends to reach the isoelectric line, but as in the case of anterior wall infarction some degree of shift of the RST segment, together with some degree of T inversion, but with Q waves in leads II and III may remain for a long time or even permanently Signs which strongly suggest posterior wall *infarction are sometimes encountered in acute pulmonary embolization* or acute pericarditis (Fig 10b)

In both anterior and posterior wall infarction, the electrocardiogram frequently shows an accelerated heart rate, extrasystoles paroxysmal tachycardia heart block, etc Goldberger[8] maintains that coronary' myocardial infarction may be diagnosed if the unipolar lead aVF shows a Q wave more than 04 second wide is accompanied by an R wave and is greater than 5 to 8 twentieths of the depth of the R wave The genesis of Q waves is not entirely clear but there is reason to believe that the wave, in precordial leads at least is the result of involvement by the infarction of the endocardial lining of the ventricular wall This forms a window for the escape of negative electrical discharge from the ventricle The negative discharge is inscribed as a Q wave

II Acute Extracardiac Conditions

The electrocardiogram in these conditions is normal even when a cardiac attack is simulated A normal electrocardiogram however is no absolute guarantee of a normal cardiovascular *apparatus If the diagnosis therefore*

* Designated also as IVF or CF4

of an acute cardiac state is strongly suspected it should not be surrendered even if the electrocardiogram is negative The electrocardiogram may not always reveal a fresh intramural infarction located strictly anterior or involving certain portions of the posterior heart wall but it can be depended upon in the greatest number of cases to show signs of previous cardiovascular damage or of an acute myocardial infarction with or without coronary occlusion

To distinguish an acute cardiac episode from extracardiac conditions which simulate it may be very difficult This difficulty arises because as already stated a generalized autonomic reaction and the manifestation of anginal pain are common to all the conditions (pp 2 19)

With respect to anginal pain the electrocardiogram registers electrical changes of cardiac conditions which are associated with pain For instance it will disclose variations in myocardial action currents caused by the pathologic events which accompany acute coronary insufficiency or acute coronary occlusion These events are associated with pain induced by anoxemia and ischemia of the heart muscle but the electrocardiogram bears no direct evidence of pain Pain that arises in the heart coronary vessels or aorta is transmitted by afferent visceral fibers to the left side of the cord at levels Th 1–4 and thence by the left 1–4 thoracic intercostal nerves into corresponding dermatomes or the pain may travel by accessory visceral pathways to other zones in the cord reaching into related extracardiac dermatomic territories

Pain engendered in an extracardiac focus sometimes takes the same route as cardiac pain the impulses of extracardiac pain passing chiefly through the cardiac cord levels (Th 1 to 4) on the left side and then into the cardiac dermatomic area (p 221) This is a simulation of anginal pain since not only is the pain of noncardiovascular origin but it is transmitted by pathways which have no connection with the coronary vessels heart or aorta *The electrocardiogram is normal*

Let us assume however that the diagnosis of an acute extracardiac state is established the accompanying pain acts like anginal pain and the electrocardiogram is not normal Are we then dealing with (1) changes in the coronary circulation induced by the extracardiac disorder (2) with pre existing cardiovascular disease or (3) with a concurrent acute cardiac episode

Gilbert and his associates[4] have claimed that afferent impulses from upper abdominal organs (gall bladder stomach) can cause vagal coronary constriction and thus initiate anginal pain But although they noted a reduction in the dog s coronary flow when the gall bladder was artificially distended and made painful[4] it is not clear that a similar mechanism operates in man when his heart and coronary vessels are normal Moreover it is not established whether this pain is anginal i e produced by change in the coronary circulation or heart muscle or whether it simulates anginal pain by reaching cardiac dermatomes by pathways having no connection with the coronary vessels and heart

A negative electrocardiogram in a young healthy subject who is stricken by an acute gall bladder attack a perforated gastric ulcer or a similar catastrophe

Acute Posterior Wall Infarction with Acute Coronary Occlusion

L M, a 68 year old male in good health for many years, was suddenly seized with agonizing epigastric and precordial pain This was followed almost at once by shock and cyanosis Bloody, frothy sputum, pointing to pulmonary infarction, appeared on the fourth day and mild jaundice on the fifth day The jaundice deepened and the gall bladder became tender and enlarged Fever and leukocytosis persisted for ten days Autopsy disclosed a recently inflamed but healing gall bladder, extensive recent involvement of the posterior wall of the heart, and acute coronary thrombosis

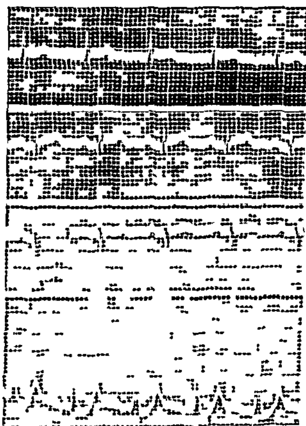


Fig 10b —The RST segment is elevated in leads I II and III and depressed in lead IV The T wave in I and III is reduced in voltage and a Q wave appears in lead II and III The elevated RST segments are suggestive of pericardial involvement

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lends support to the premise that, despite the development of sinistral pain which simulates anginal pain, the coronary circulation and heart were not involved and the sensory impulses of pain passed through the neuraxis without touching the cardiovascular apparatus Electrocardiographic signs of acute *coronary insufficiency, on the other hand, would be open to the interpretation* that the coronary circulation had been affected as in the case of the dog with a normal coronary circuit and a distended painful gall bladder

Except in the cases of acute coronary insufficiency induced by severe generalized causes such as great loss of blood or acute CO poisoning, abnormal electrocardiographic findings in young healthy subjects afflicted by an acute extracardiac state are rare

Acute pulmonary embolization can, however, produce acute coronary insufficiency with corresponding electrocardiographic signs in individuals who possess normal heart muscle and coronary vessels This is illustrated by the case described in Figure 3

Some observers[1, 13] have explained the coronary disturbance following pulmonary embolization as a pulmono coronary reflex Scherf and Schonbrunner[10, 11] published records which appear to confirm this, Eckardt,[3] however, was unable to substantiate the existence of such a reflex, and more recently, Parin[8] has been unwilling to accept it Be this as it may it may be inquired what mechanism and pathways play a part in producing anginal pain in acute explosive conditions of an abdominal organ, for instance Are there afferent vagal pathways which lead from an inflamed gall bladder or pancreas or from a perforated hollow viscus to the neuraxis and then to the coronary vessels? Do afferent vagal nerves from these and other organs go to the sympathetic gangliorated chain (to the superior cervical ganglion [Coffey and Brown]) where they may be relayed to efferent coronary constrictors? Are axon reflexes involved? These questions cannot be answered at present since it is not universally accepted that afferent vagal fibers carry pain from the heart and coronary vessels, and *that the latter are constricted by vagal nerves*

Older subjects are generally suspect of having some degree of cardiovascular impairment and this is usually confirmed by electrocardiographic findings But suspect or not an acute extracardiac event will produce in the electrocardiogram no disturbance at all or no change beyond that associated with old cardiovascular events, or it will produce changes of acute coronary insufficiency or of a fortuitous concurrent acute coronary occlusion The case record of L M (p 22) is that of a man who suffered concurrently from acute coronary occlusion with myocardial infarction and an attack of acute cholecystitis

Severe and recurrent anginal pain may be accompanied by no electrocardiographic alterations This is illustrated by the two cases described on p 52 Or the electrocardiographic changes of angina pectoris with anginal pain may appear only when the impulses of anginal pain are summated by impulses of pain derived from some extracardiac focus This is seen more *especially in*

patients with coronary sclerosis and old healed heart damage Whereas prior to the extracardiac episode the cardiovascular apparatus may have produced only a small quantity of sensory impulses which were subclinical i e insufficient to initiate anginal pain after the extracardiac episode sensory impulses from the active noncardiac lesion join with the other group of impulses to produce anginal pain as an overt manifestation A subacromial bursitis a smoulder in gall bladder and other extracardiac foci can act in this way

The same phenomenon is indirectly illustrated by the improvement or disappearance of anginal pain in heart disease when a troublesome extracardiac lesion e g a diseased gall bladder is removed Amelioration of anginal pain following local anesthetization of a local patch of skin on the left arm (Weiss and Davis[14]) is another example of the same principle

The electrocardiogram may show no change at all with the onset development or disappearance of anginal pain under the circumstances described above unless produced by the coronary circulation

BIBLIOGRAPHY

[1] Burch G and Winsor T A Primer of Electrocardiography Philadelphia Lea & Febiger 1945

[2] Coffey W B and Brown P K The surgical treatment of angina pectoris Arch Int Med 1923 31 200

[3] Eckardt P Zur Frage pulmocoronarer Reflexe bei Lungenembolie Pfluger s Arch 1938 241 224

Gilbert N C Fenn G K and LeRoy G V The effect of distention of abdominal viscera on the coronary blood flow J A M A 1940 115 1962

— LeRoy G V and Fenn G K The effect of distention of abdominal viscera on the blood flow in the circumflex branch of the left coronary artery of the dog Am Heart J 1940 20 519

[6] Goldberger E Unipolar Lead Electrocardiography Philadelphia Lea & Febiger 194

Katz L N Electrocardiography Philadelphia Lea and Febiger 1946

[8] Parin V V The role of pulmonary vessels in the control of the blood circulation Am J M Sc 1947 214 16

Scherf D and Boyd L J Clinical Electrocardiography St Louis C V Mosby 1941 2nd edition Philadelphia Lippincott 1946

[10] — and Schönbrunner E Über Herzbefunde bei Lungenembolien Ztschr f Klin Med 1935 128 4

[11] — and — Über den pulmocoronaren Reflex bei Lungenembolien Klin Wchnschr 1937 16 340

[12] Strueff N Zur Frage der bakteriellen Lungenembolie Virchows Arch 1909 198 211

Villaret M Justin Besançon L and Bardin I Physio pathologie des accidents mortel consécutifs aux embolies pulmonaires Bull et mém Soc méd d hôp de Paris 1936 § 956

— — and — Recherches sur la prévention expérimentale des accidents consécutifs aux embolies pulmonaires Bull et mém Soc méd d hôp de Paris 1936 52 941

Weinstraub H J and Bishop L F Jr The anoxemia test for coronary insufficiency Ann Int Med 194 26 41

[14] Weiss S and Davis D The significance of the afferent impulses from the skin in the mechanism of visceral pain Skin infiltration as a useful therapeutic measure Am J M Sc 1928 176 517

SECTION TWO

Physiological Aspects

CHAPTER IV

General Autonomic Regulations

General Considerations

ALL BRANCHES of medicine and more especially internal medicine and neurology share a common territory which may be regarded as a repository of the autonomic regulations of the body The study of this common ground is in effect the study of the autonomic nervous system The many patterns of clinical disease are partially or wholly expressions of autonomic activity and this activity may or may not be associated with somatic alterations These considerations will be better appreciated with an understanding of the general physiology of the autonomic nervous system

To a very appreciable degree the autonomic and somatic nervous systems are interdependent although the autonomic system enjoys a considerable autonomy of its own However this autonomy operating in a coordinated manner to maintain the intrabodily environment at an optimal functional level (Bernard[11, 18] milieu interieur Cannon[27] homeostasis Jelliffe[?] homeokinesis) is not entirely complete By devices of its own the autonomic nervous system in general subservient to the cerebrospinal system exercises important regulations over intrabodily processes Nature has seen to it that these regulations are not easily put out of commission Man can partly influence these regulations but short of self-destruction he cannot deflect or stop their inherent autonomicity

Examples of independent reflex action and of the autonomic activities affected by psychic influences or by volitional factors are given below

A Psychic Influences and Autonomic Reactions

Autonomic acts may be modified by will power to a certain extent but in the main the autonomic activities remain outside volitional influences On the other hand the vegetative *functions are quite readily affected by* emotional states For the psychologist and the practicing physician the problem is still unsettled whether emotions are the *consequence* of somatic (including autonomic and endocrine) reactions or whether these reactions are *initiated by* emotional or psychic activities This is a dispute beyond our immediate interest However an allusion to the *variations in the behavior* of organs for example of the heart stomach and intestines associated with abnormal play of emotions is within the province of our discussion Palpitation loss of

appetite, hyperchlorhydria and diarrhea are observed with many emotional derangements especially apprehension, fear, or excitement, other instances are blushing (as in shame), clammy, cold perspiration (as in sudden embarrassment), disturbances in sleep or in staying awake (in mental distress), the onset of jaundice (from intense anger or fright), and even imaginary pregnancy (Hoff[70]) (*For a fuller discussion of this subject consult Wittkower,*[145] Mc Gregor[97] Dunbar[49] Spiegel,[136] Kennard[74] and Kuntz [79])

Cortical, i e, psychic processes, can intensify and aggravate the clinical manifestations of disease Angina pectoris ulcers of the gastro intestinal tract, disease of the liver and bile ducts belong in this category, also autonomic manifestations associated with localized damage of a related area in the cortex, i e, hemiplegia, jacksonian epilepsy, Quincke's edema, Raynaud like vascular peripheral changes, and scleroderma The cortex exercises an influence upon cardiovascular and metabolic activities, on temperature, and on gastro intestinal and other regulations The association of psychic states with the sudden onset of Graves' disease, glycosuria, diabetes mellitus, and diabetes insipidus *is recognized*

B Intrinsic Reflex Centers

In contrast to the somatic innervations the autonomic system, it has been asserted, lacks peripheral centers in which reflexes take place but this is not altogether a valid premise The cells of the enteric system, for example, may be regarded as reflex centers, they mediate coordinated reactions of the intestines independently of the central nervous system Other organs possess intrinsic reflex centers

C Axon Reflexes

Another type of reaction the so called axon reflex known as the Sokownin reflex is often cited as an illustration of an autonomic reflex although strictly speaking this is a pseudo not a genuine reflex The reflex is really an extraspinal shortcut ' mediated between two structures or organs the efferent *neuron* to each structure coming off a common trunk Bruce [5] postulated the existence of such a reflex in connection with cutaneous blood vessels and in connection with inflammatory conditions The ' reflex was at least suspected by Claude Bernard [15] Sokownin[133] described the reflex Langley and Anderson[84] analyzed its mechanism, Speranskaja Stepanowa[134, 135] observed reactions analogous to the axon reflex in the frog and Wernøe[141] in fishes Hryntschak and Spiegel[77] found that the reflex could be transmitted by the pelvic nerve while Breslauer [3] drew attention to this reflex in man as a localized reaction in the skin

The bearing of axon reflexes upon many clinical manifestations deserves further study As is well known Lewis[87] and others invoke this reflex to explain *the local response* of the skin arterioles and capillaries to histamine But this type of reflex may underlie other autonomic manifestations For instance the

radiation and reference of gallbladder pain into the stomach or vice versa is perhaps mediated by nervous pathways which do not extend beyond an intra abdominal autonomic ganglion (Fig 11) A similar mechanism may hold for vasomotor and secretory activities within the abdomen or other territories of the body

Manifestations Projected by the Autonomic Nervous System

More significant than the problematic existence of an intrinsic reflex are the mass action (p 15) and the universal way in which the autonomic system

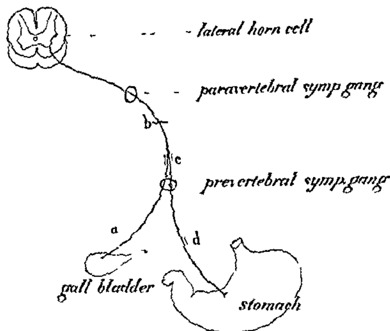


Fig 11 — Schema of an Axon Reflex Between Gall Bladder and Stomach A stimulus from a (gall bladder) goes no higher than b then descends along c and d to reach the stomach

responds The mass action is probably inaugurated at the sources of origin of the vast groups of efferent fibers these sources are the nuclear condensations and other related structures situated in the brain stem (diencephalon mesencephalon pons and medulla) in the telencephalic region and even in the spinal cord itself From these centers the discharge of impulses is constant but varies under abnormal conditions Under all circumstances however these discharges are promptly transmitted through a multitude of efferent (centrifugal) neurons reaching into the tiniest recesses of the body and sympathetic (adrenergic) or parasympathetic (cholinergic) manifestations are set off according to the autonomic division brought into play

A Sympathetic Innervations and Their Manifestations

The sympathetic afferent (sensory) fibers are concerned primarily with the transmission of impulses of pain into the neuraxis The efferent fibers emerge from the neuraxis and transmit efferent impulses into the viscera and peripheral structures

1 *Peripheral To Blood Vessels, Sweat Glands, Erector Pili Muscles, and Structures of the Head*

Generally speaking, the peripheral manifestations consist of reactions on the part of the blood vessels, sweat glands, and erector pili muscles As a result of constant discharge of constrictor impulses to the muscular walls of the arterioles, the peripheral vascular beds are kept in a sustained state of contraction i e, tonicity

Whereas the blood vessels of nearly all the internal organs possess sympathetic and parasympathetic nerves the *peripheral blood vessels* appear to receive their innervation from the sympathetic division alone (Fig 13) Parasympathetic nerves have not been definitely established (Kure[80–83] opposite contention in connection with skeletal blood vessels) At any rate, stimulation of the sympathetic fibers to vessels of the extremities causes constriction of arterioles (Bernard[1 13]), and capillaries (Doi[4]) Variation in the lumen of the vessels is supposed to be accomplished by an increase or diminution of sympathetic influences

Similarly the *sweat glands* also under sympathetic control apparently possess no parasympathetic nerves The sympathetic nerve endings to sweat glands behave like parasympathetic (cholinergic) nerve endings these endings and the sweat glands will not respond to adrenalin This would seem to illustrate an exception to the rule that adrenalin always causes a sympathomimetic action Erector pili muscles too, are under motor sympathetic control and seem to have no parasympathetic nerves

The *cephalic region* is supposed to be without sympathetic afferent fibers at least none have been conclusively demonstrated In the absence of sympathetic afferent communications pain in this territory has been explained on the basis that afferent impulses which may reach the superior cervical sympathetic ganglion stimulate intraganglionic cells from these efferent neurons go to the head region causing constriction of blood vessels and other sympathetic manifestations According to Livingston[89] constriction of the cerebral vessels the middle meningeal artery will cause pain this presupposes the existence of an intracranial afferent nerve supply Whether or not any of these explanations hold water there is no doubt of the ground upon which physiologists stand with respect to the function of the efferent sympathetic neurons in the head region The iris of the eye Muller s muscle the upper eyelid and

blood vessels, sweat glands, etc., in the skin of the head are controlled by sympathetic supplies.

To the sympathetic innervation of Müller's muscle and of the retrobulbar fat pad is attached a special interest in connection with experimental and clinical exophthalmos. Whether the sympathetic nerves actually participate in the production of exophthalmos is not clear. Bearing on this query are the studies of Miller and Taub[99] who, by the intravenous injection of oxyquinoline, were able to induce acute and pronounced bilateral exophthalmos in rabbits, a result which failed to appear when the animal was under anesthesia. Extirpation of the cervical sympathetic ganglion did not prevent the onset of exophthalmos. (See Marine[93, 94] and Marine and Rosen[95] for studies on chronic exophthalmos induced experimentally.)

The persistence and even the aggravation of exophthalmos after thyroidectomy has also been noted in patients who remained greatly improved and apparently free of unusual autonomic manifestations. This type of persistent exophthalmos has been explained on the basis of an excessive sympathetic discharge through sympathetic nerves which supply the structures of the eye. However, this concept is not altogether satisfactory.

The absence of exophthalmos in quite a number of instances of frank and advanced thyrotoxicosis is no less difficult to understand. While the cause of exophthalmos is still an enigma, we should like to suggest that the occurrence of exophthalmos in man may be contingent upon the existence of an adequate quantity of Müller's fat behind the orbit. This fat *in man* is a vestigial structure and varies in amount from individual to individual. When it is scant to begin with, even were it to hypertrophy, as is often the case during the state of thyrotoxicosis, it might not be able to hold the eyeball forward.

7. Visceral: To Bronchial Musculature, Pulmonary Vessels, Bronchial Arteries, Coronary Vessels, Heart, Abdominal and Pelvic Viscera

The *bronchial musculature* is supplied by dilator fibers.

The *pulmonary vessels*, it is safe to say, *receive* sympathetic nerves. The nerves to the lung vessels have long been a troublesome and confusing subject of study, especially for the clinician. Even at the risk, therefore, of extending this discussion beyond our original intention, the pulmonary innervation will be reviewed at some length. (For parasympathetic supplies, see p. 69.)

In earlier investigations, the existence of pulmonary vasomotor nerves was either denied or their function looked upon as slight or inconsequential. Bradford and Dean[6, 22] obtained a rise in pulmonary blood pressure by stimulating the peripheral cut ends of thoracic nerves 3, 4, 5 and probably of 6 and 7. Wood[148–149] reported similar results. François-Franck[53] also confirmed this. Plumier[108–109] reported that stimulation of vasomotor nerves to the lungs of dogs led to an increase in pulmonary blood pressure, but Brodie and Dixon[24]

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In a more recent study employing an innervated Starling heart lung preparation with separate perfusion of the heart Gollwitzer Meier and Kruger[38] found that stimulation of the sympathetics caused an increase in pulmonary blood pressure due to vasoconstriction whereas stimulation of the vagus produced a decrease in pulmonary blood pressure due to vasodilatation

Although adrenalin became established as a useful chemical tool for the detection of the pulmonary vasomotor innervation the experimental results were not the same in all hands Velich[135, 136] and Gerhardt[54] obtained no pulmonary vasoconstriction Brodie and Dixon[4] published similar results they observed slight dilatation even with large doses of adrenalin Heger and Philippson[67] Heymans and Vercoullie[65] in the rabbit and Tribe[133, 134] reported dilatation which followed constriction Moller[100] Baehr and Pick[4] and *Hirakawa*[67] contended that vasoconstriction of the pulmonary vessels is absent after the introduction of adrenalin Other authorities like Cybulski[36] and Petitjean[108] claimed that with adrenalin pulmonary vessels underwent a passive dilatation whereas Krawkow[3] and Weber[140] held that the pulmonary vessels exhibited a direct active dilatation from adrenalin

The divergence in these results was laid to differences which characterize the reactions of various animals and to differences in the character of the perfusion fluids The pH concentration and the quantity of calcium as well as the temperature of the fluids proved to be important factors and the quantity of adrenalin employed no less important Variations in the amount of adrenalin was held to be the chief cause of the inconstant results (Tribe[134] Romm[114] and De Burgh Daly[42])

A matter of some interest in the light of studies on experimental pulmonary embolization (Strueff[127] Villaret et al[137, 138] Scherf and Schonbrunner,[117, 118] and Eckardt[49] who was unable to substantiate the existence of a pulmonocoronary reflex) and on the clinical relationship between pulmonary and coronary circulations in man is that in practically all the experimental studies on pulmonary arterial pressure little attention was paid to the coronary dilatation which accompanied the use of adrenalin nor was the coronary dilatation associated with change in pulmonary tension considered to be of any import Later on investigators working with adrenalin perfusion experiments remedied this oversight

The *bronchial arteries* it is held are *constricted* by thoracic sympathetic nerves and are alleged to be supplied by *sympathetic* vasodilators Hovelacque[73] stated that in man sympathetic twigs which accompany the bronchial arteries usually arise from the ganglia of Th 3 and 4 Perfusing the lungs through the bronchial arteries with adrenalin will cause an increase in bronchial arterial pressure Vasomotor sympathetic constrictor nerves to these vessels have been described and discussed by De Burgh Daly[4] [43] De Burgh Daly and von Euler[44] and Rjasanskij[113]

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as well as Erikson,[51] Weber[140] and Lohr[91] denied this. In Tribe's experience,[134] however, stimulation of the stellate ganglion induced constriction followed by dilatation. LeBlanc and van Wyngaarden[83] were able to cause constriction of pulmonary vessels by stimulating the stellate ganglion in the cat, and vasodilatation by stimulating the vagus nerve. Confirmatory proof of the existence of pulmonary vasomotor nerves was brought forward by DeBurgh Daly and von Euler.[44] Their results were not uniform but they demonstrated, nevertheless, that excitation of the thoracic vagosympathetic nerves in the dog produced vigorous constriction or weak dilatation, dilatation they attributed to a cholinergic effect. Others who turned to this problem were Dixon and Hoyle,[45–47] Berry, Brailsford and DeBurgh Daly,[1] and especially De Burgh Daly and von Euler. These last, working with dogs and acting on the suggestion made by Berry et al., ingeniously maintained the blood supply to the nerve heads of the pulmonary vasomotor nerves by simultaneously perfusing the bronchial as well as the pulmonary arteries. This procedure kept alive the vasomotor nerves, enabling them to function.

The evidence from all this research was definitely in accord with the belief of a nervous control of the lung vessels. Vasoconstriction, for mammals at least it seemed reasonably certain, was a sympathetic reaction and it also became apparent that the pulmonary vessels were in a tonic state of constriction.

The proof of vasoconstrictor activity of nerves to the pulmonary vessels secured a broader and better foundation when adrenalin was added to the experimental procedure of investigations. Over fifty years ago this substance, then designed as adrenal extract, was known to produce an increase in pulmonary pressure. Cybulski[36, 37] and Szymonowicz[1, 5] believed that extracts of the adrenal gland caused a generalized vasoconstriction as a result of a central action. Later Pilcher and Sollmann,[105] as well as Kolm and Pick[77] showed this concept to be erroneous, but the Polish investigators evidently understood that adrenal extract could produce pulmonary vasoconstriction. After them Plumier,[10] Meyer,[93] Langendorff,[84] Wiggers,[143] Barbour,[5] Petitjean,[107] Tribe[133] and Romm[114] recorded the constriction of lung vessels by adrenalin. Campbell[6] observed constriction in dogs and rabbits, Fuhner and Starling[54] constriction in the dog, Schafer and Lim,[116] Lohr[91] and Schlesinger[119] constriction in the cat which was occasionally followed by dilatation. Pick[104] and Petitjean claimed that the intravenous injection of nitrites produced pulmonary vasoconstriction but this was denied by Plumier.[108, 109]

Gollwitzer Meier, Kramer and Kruger[57] published studies on denervated heart lung preparations, demonstrating that the increase in pulmonary pressure following adrenalin was in part due to increase in cardiac minute volume output, the prolonged rise in pulmonary pressure was due to vasoconstriction of the pulmonary vessels. Most of the investigators worked with Starling heart preparations, a method which permits rather trustworthy analysis of the factors underlying pulmonary pressure, since the element of venous return is excluded.

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probably dilator in nature (Fig 13) The existence of a coronary dilator innervation, in contrast to a sympathetic constrictor supply to peripheral vessels, is upheld by physiologists like Anrep and Segall, Hochrein and Keller,[69] Langendorff,[81] Rein,[111] and Wiggers [141] In general, they emphasize the significance of the vagal constrictors, whereas Katz and Jochim[73a] hold an opposite view Greene,[59–6] Gollwitzer Meier and Kruger,[53] and Hinrichsen and Ivy[67] especially, stress the predominant tonic action of sympathetic dilators on coronary arteries A number of authorities, however, claim that the coronaries are constricted by sympathetic nerves, and these nerves, it is alleged travel in the superior sympathetic cardiac nerves On the basis of this assumption section of these nerves has been carried out to interrupt and prevent constriction of the coronary vessels (Coffey Brown and Humber,[3] and Kerr[75] [6]) But controversial and conflicting results (Richardson and White,[11] White[14]) have made it difficult to accept a sympathetic vasoconstrictor innervation to the coronary vessels, at least without strong reservations

The *heart* is supplied by cardio accelerator sympathetic fibers (Fig 18) Thoracic in location, these emerge from the upper thoracic spinal cord segments In addition to these cardio accelerator fibers of thoracic origin, Beattie Brow and Long[7–9] described a group of efferent sympathetic neurons which leave the posterior hypothalamic area and descend intraspinally to the upper thoracic segments of the cord where the neurons relay to the stellate ganglion and then to the cardiac plexus This newly discovered group of hypothalamo spinal fibers is an upper neuron pathway for cardiac regulation, with a direct influence on cardiac rhythm (Fig 24)

The *abdominal viscera* are innervated by a major portion of the sympathetics (Fig 3) This large abdominal sympathetic division sends (a) inhibitory fibers *to the smooth muscles of the alimentary tract, (b) secretory* fibers to the adrenals (c) constrictor and vasodilator fibers to the vast splanchnic vascular beds (see Tomb[131] for sympathetic vasoconstrictor effects on the splanchnics) (d) fibers to the adrenals kidneys spleen liver and pancreas In the case of the kidneys *for example an autonomic supply to the vascular components* is generally accepted but an autonomic innervation to the tubular apparatus is not established (Smith[120])

Sympathetic vasoconstrictor fibers supply the blood vessels of the *pelvic viscera* for example causing rapid emptying of blood of the external genitalia Interesting is the reported absence of autonomic nerves to the placental blood vessels and their ability to become relaxed (dilated) in the presence of low O_2 or high CO_2 tension in the blood (Schmitt[110, 111])

3 *General Effects**

There are also central autonomic manifestations These appear as changes in metabolism, temperature water regulation and the sleep-waking mecha

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nism in emotionality etc and in associated endocrine activities Morphologic changes in the blood elements (an increase in the total number of leukocytes and of immature neutrophilic forms) have also been described

B Parasympathetic Innervations and their Manifestations

In general these seem to be antipodal or antagonistic to the sympathetic manifestations (p 64) The parasympathetic manifestations are also peripheral (regional) and general The peripheral effects are discussed below

1 *Regional and Visceral Manifestations*

The *head* has constrictor fibers which go to the ciliary body of the eye the pupillary sphincter and secretory fibers supply the submaxillary and parotid glands

The thorax contains a large parasympathetic supply constrictor fibers innervate the *bronchial musculature* and according to McDowll[96] these muscles also receive a vasodilator supply from the parasympathetic system As a clinical illustration of an almost selective reaction on the part of the bronchial constrictor mechanism relieved by the effect of adrenalin acting on the bronchial sympathetic dilators the following case is cited

M S a 60 year old male at Montefiore Hospital had had hypertension for a number of years associated with repeated episodes of precordial distress and dyspnea He was known to have had multiple cardiac infarctions associated with coronary occlusions and he eventually developed signs of chronic circulatory failure During a later episode of paroxysmal nocturnal dyspnea accompanied by precordial pain he developed diffuse rhonchi and moist rales over the entire chest *He seemed to breathe* like a patient in an attack of asthma He became cold and clammy and his dyspnea grew very severe The blood pressure before and *after this* attack remained unchanged Despite the background of his coronary and cardiac disease he was given a dose of adrenalin he was immediately *relieved of his* dyspnea and general distress and the signs in his chest cleared.

The parasympathetic supplies to the *pulmonary vessels* are still not clearly established Henriques[64] suggested that the vagus carries vasomotor nerves to the lungs and von Euler[5-] was reasonably certain these nerves were vasoconstrictors When he stimulated the vagus nerve the blood vessels became constricted this effect was increased by *eserine* and *reduced by* atropine Together with De Burgh Daly[41] he demonstrated that excitation of the thoracic vagosympathetic nerves in dogs led to vigorous pulmonary vasoconstriction or to weak vasodilatation the vasodilatation was considered a cholinergic effect Vasodilator fibers that are parasympathetic have been described by Anderson[1] and Prevost and Saloz[110] and McDowall[96] has maintained that the pulmonary vessels probably receive parasympathetic vasodilators In unpublished per

creased output of cells consisted of neutrophilic leukocytes and this response often but not always paralleled the *elevation in* temperature Occasionally there was an increase *in* polychromatophilic red blood cells and an occasional normoblast appeared These results call for further investigation especially since the sites of damage were not clearly defined

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in favor of the contention that the pulmonary vessels undergo cholinergic vasodilatation

The *bronchial vessels* are not known to possess parasympathetic nerves vasodilatation being attributed to sympathetic fibers (p 67)

Inhibitory fibers go to the pacemaker of the *heart* (Fig 18)

Vasoconstrictor fibers supply the *coronary vessels* (Anrep and Segall[2] Rein[111] Collwitzer Meier and Kruger[38] and Wiggers[144])

The *abdomen* receives fibers which innervate the smooth muscles and glandular structures of the alimentary tract down to the ileocolic valve Parasympathetic fibers go to the kidneys spleen pancreas and other abdominal organs (Fig 12)

The *pelvis* contains motor fibers which regulate the evacuation activities of the colon rectum and bladder The external genitalia become engorged with blood (erection) as a result of parasympathetic vasodilatation of blood vessels to these organs (Fig 12)

2 *General Effects*

General parasympathetic manifestations are induced by the action of central parasympathetic mechanisms These manifestations may be noted as a generalized fall in blood pressure depression of the respiration disturbances of bladder gastro-intestinal or other functions The parasympathetic division also has an influence on metabolism secretory activities osmotic pressure of bodily fluids, and the regulation of blood elements (eosinophils and lymphocytes) It is probably an oversimplification to designate patients as vagotonic or sympathicotonic and a similar criticism may be leveled at any attempt to label central autonomic activities like temperature regulation sleep-waking rhythm or water exchange as either parasympathetic or sympathetic in nature

Anatomic Pattern of Ganglia, Neurons and Plexuses as a Determinant of Physiologic Behavior of the Autonomic Nervous System*

The anatomic origin of peripheral neurons is different for each division of the vegetative nervous system The sympathetic efferent fibers arise in the spinal cord from bilateral parallel continuous columns of cell bodies lying in the gray matter of the lateral horns from C 8 to L 2 (Fig 12) On leaving the spinal cord the preganglionic neurons are soon relayed at a synaptic junction in a ganglion (lateral or collateral as a rule) from this point the distal postganglionic neurons continue for a considerable distance eventually arriving at a viscus or a peripheral effector

The parasympathetic efferent fibers on the other hand originate in isolated clusters of cell bodies scattered through the craniobulbar and sacral cord levels (Fig 12) The preganglionic neurons comparatively long continue until the

* See Chapters VI through IX for description of the anatomy

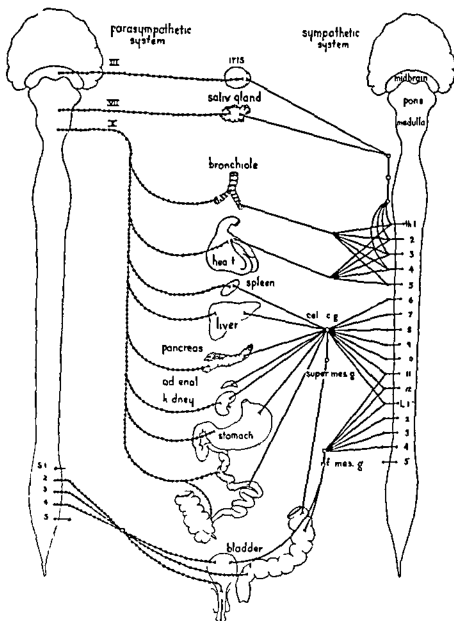


FIG 12 — Autonomic Innervations to the Organs of the Body For schematic purposes each autonomic division is represented as coming off a separate neuraxis The parasympathetic cranial outflow is by way of the IIIrd VIIth IXth Xth XIth cranial nerves the sacral outflow by way of S 2 3 4 Hair sweat glands and blood vessels to the skin of each dermatomic area of the body are supplied by sympathetic fibers arising at the neuraxial levels related to each dermatome in question These fibers are omitted For innervations to the peripheral and visceral blood vessels see Fig 13

fusion experiments he found that acetylcholine constricted the pulmonary vessels in the cat On the whole, all the evidence thus far seems to be strongly

reservations in some quarters Elliott[38] was the first to suggest that chemicals play a part in the propagation of nerve impulses About three decades later Loewi[40] also Dale[35, 39] and Dale and his co-workers[40] were able to confirm this theory by factual evidence

While it is not absolutely established that chemicals actually transmit impulses across synapses no one disputes the presence and the general physiologic attribute of the chemicals—adrenalin and acetylcholine—in connection with the autonomic innervations

A ADRENALIN

Adrenalin as we shall see has an important place in the activities of the autonomic nervous system The physiologic and pharmacologic properties of this substance are well known The adrenal glands are supplied by (sympathetic) preganglionic neurons but have no postganglionic neurons, for this lack adrenalin itself serves as a substitute or equivalent Upon stimulation the medullary portion secretes adrenalin and delivered into the blood stream and carried through the body this substance it is believed sets off adrenergic responses at adrenergic reacting nerve endings At once and on a large scale the individual is provided with a fluid postganglionic acting agent and as a consequence the body acquires an ability to supplement and enhance its normal constant discharge of sympathetic impulses The level of adrenalin however is regulated and kept within bounds An excess is immediately halted by the readiness with which this substance is oxidized in the tissues and albeit somewhat more slowly even in the blood Probably other endocrine substances contribute to autonomic activities but the action of adrenalin in this respect is understood best

In many respects resembling adrenalin but not identical with it is a chemical product elaborated and liberated at the nerve endings of sympathetic postganglionic neurons To this product Cannon[9] and Cannon and Rosenblueth[?] have given the name sympathin According to them two varieties exist (a) sympathin E produced during sympathic contraction of smooth muscles elsewhere causing only motor or excitatory reactions and (b) sympathin I produced in muscles relaxed by sympathetic stimulation elsewhere causing only inhibitory effects Not all authorities accept this separation into two kinds of sympathin e g Loewi[40] Bacq[1] The latter for example agrees with Elliott s opinion that sympathin and adrenalin are identical

More recently again Cannon and Lissak[20] emphasized the difference between adrenalin and sympathin Their view is that adrenalin is liberated at the ends of the adrenergic fibers and that sympathin which escapes from the stimulated region into the blood stream is this adrenalin modified in the affected cells Furthermore they found that extracts of adrenergic fibers whether from the mesenteric nerves or from organs containing these nerves acted like adrenalin

reach a ganglion close to (or within) the very organ they supply As a consequence, a postganglionic neuron has but a short distance to go in order to reach an organ or an effector Sometimes the postganglionic neuron has its source, course and termination within a single organ or effector This type of post ganglionic fiber distribution makes it possible for this division to act on a single organ without at the same time affecting other organs This discrete or fractional type of response differs from the diffuse and general action elicited by the sympathetic division, (Cannon [7, 8])

Very probably both divisions possess identical architectural arrangements with respect to the synaptic connections between the first or preganglionic neuron, and the second or postganglionic neuron In the sympathetic division the synaptic connections have been carefully investigated in recent years by *Billingsley* and Ranson [19] This general arrangement seems to have been known to Bidder and Volkmann [18] Billingsley and Ranson were able to count in the *superior cervical ganglion of the cat thirty two postganglionic neurons affecting* a contact with a preganglionic neuron Furthermore, sympathetic preganglionic neurons in general have a dendritic arborization in multiple sympathetic ganglia *of the paravertebral chain above or below the level of emergence* of the preganglionic fibers reaching from six to nine ganglia All this is conducive to an effective transfer of preganglionic impulses into a diffuse and profuse outlying galaxy of postganglionic fibers

Whereas both divisions share commonly in the formation of numerous small plexuses and in more prominent plexuses as well no actual fusion or anastomoses between the fibrils belonging to each division has ever been demonstrated As a general rule the sympathetic network is carried by vascular channels *but it has not yet been established whether the tiny fibrils of these* circum vascular plexuses innervate the smallest capillaries of every circuit (see Woollard[149] in reference to coronary arterioles) On the whole, nerve fibers of both divisions supply every part of the body and are especially prominent in the celomic cavities

Participation of Chemical Transmitter Substances in Physiologic Responses of the Autonomic Nervous System

Just how the axons of the autonomic and somatic innervations carry impulses is still a matter of considerable mystery The problem has been subjected to two lines of attack The older view held that nerve excitation is transmitted by an action current *in the nerve in other words that a succession of excitatory* impulses is initiated by a potential difference between an active and an inactive region of a segment of nerve The newer school of physiologists claims that nerve impulses may be transmitted by chemical substances across synapses and at nerve endings These two points of view are not necessarily irreconcilable but the second hypothesis—the concept of chemical transmitter agents—has in recent years received almost exclusive emphasis though not without raising

reservations in some quarters. Elliott[30] was the first to suggest that chemicals play a part in the propagation of nerve impulses. About three decades later Loewi[8], also Dale[25, 29] and Dale and his co-workers[40] were able to confirm this theory by factual evidence.

While it is not absolutely established that chemicals actually transmit impulses across synapses, no one disputes the presence and the general physiologic attributes of the chemicals—adrenalin and acetylcholine—in connection with the autonomic innervations.

A. Adrenalin

Adrenalin, as we shall see, has an important place in the activities of the autonomic nervous system. The physiologic and pharmacologic properties of this substance are well known. The adrenal glands are supplied by (sympathetic) preganglionic neurons but have no postganglionic neurons. For this lack adrenalin itself serves as a substitute or equivalent. Upon stimulation the medullary portion secretes adrenalin and, delivered into the blood stream and carried through the body, this substance, it is believed, sets off adrenergic responses at adrenergic reacting nerve endings. At once and on a large scale the individual is provided with a fluid postganglionic acting agent and, as a consequence, the body acquires an ability to supplement and enhance its normal constant discharge of sympathetic impulses. The level of adrenalin, however, is regulated and kept within bounds. An excess is immediately halted by the readiness with which this substance is oxidized in the tissues and, albeit somewhat more slowly, even in the blood. Probably other endocrine substances contribute to autonomic activities, but the action of adrenalin in this respect is understood best.

In many respects resembling adrenalin but not identical with it, is a chemical product elaborated and liberated at the nerve endings of sympathetic postganglionic neurons. To this product Cannon[9] and Cannon and Rosenblueth[22, 23] have given the name sympathin. According to them, two varieties exist: (a) sympathin E, produced during sympathic contraction of smooth muscles, elsewhere causing only motor or excitatory reactions, and (b) sympathin I, produced in muscles relaxed by sympathetic stimulation, elsewhere causing only inhibitory effects. Not all authorities accept this separation into two kinds of sympathin, e.g., Loewi,[80] Bacq.[3] The latter, for example, agrees with Elliott's opinion that sympathin and adrenalin are identical.

More recently again, Cannon and Lissak[30] emphasized the difference between adrenalin and sympathin. Their view is that adrenalin is liberated at the ends of the adrenergic fibers and that sympathin, which escapes from the stimulated organ into the blood stream, is this adrenalin modified in the affected cells. Furthermore they found that extracts of adrenergic fibers, whether from the mesenteric nerves or from organs containing these nerves, acted like adrenalin

or had the characteristics of adrenalin By way of contrast, extracts of vagus nerves and skeletal muscle, or of the heart in which sympathetic fibers have been permitted to degenerate possessed none of the attributes of adrenalin as exemplified in its effect on blood pressure or on the iris of the eye Over forty years ago, Lichtwitz[93] suggested that adrenalin may be transmitted in the axon cylinders in much the same way as tetanus toxin, for instance, and Elliott[50] at about the same time (1904), postulated that sympathetic nerve impulses released minute amounts of an epinephrine like substance, and he considered this release a chemical step in the process of stimulation

With notable exceptions the terminal nerve endings of all sympathetic post ganglionic neurons react to adrenalin and, according to the Harvard school of physiologists, to an adrenalin like substance sympathin For fibers which behave in this way, Dale coined the term adrenergic

B ACETYLCHOLINE

This substance known to exist outside the body, is also endogenous It has been found at all intraganglionic relays between the first or preganglionic neuron and the second, distal or postganglionic neuron It has also been found at the terminal nerve endings of parasympathetic postganglionic fibers Whereas its distribution in the efferent system of the autonomics is general the chemical has not been detected as yet in any of the afferent neurons or at the synaptic junction which these afferent neurons make within the gray matter of the cord On the other hand acetylcholine has been found in somatic nerves and in sympathetic as well as in parasympathetic ganglia (de No[41])

The identification of intrabodily acetylcholine is a comparatively new discovery Loewi found that this substance was liberated by the vagus Later it was identified not only at synaptic junctions in the parasympathetic division, but also at synaptic connections between pre and postganglionic neurons in the sympathetic divisions and in somatic nerves also (de No) As in the case of adrenalin a regulatory quantitative balance seems to prevail for acetyl choline The drug is destroyed rapidly by an enzyme cholinesterase in the blood and tissues (Nachmansohn[101]) and the destruction of this chemical by esterase is checked or prevented by the action of physostigmine Dale[39] has extended many of these observations Acetylcholine has been identified not only during bodily (somatic) reactions but also it appears during emotional states of fright or fear (Bender[10, 11])

Neurons which react to acetylcholine have been designated by Dale[39–40] as cholinergic in contradistinction to the adrenergic acting neurons As a rule, adrenergic and cholinergic fibers are confined respectively to the sympathetic or parasympathetic divisions But anatomic interplacements or interlacings occur, that is to say cholinergic fibers have been discovered within the sympathetic division and quite probably adrenergic fibers exist within the parasympathetic division Testut[1, 9] found fibers of both divisions in the same tract

and the probability that vagal fibers (cholinergic) run in the sympathetic cord served Tigerstedt[130] as the basis for his explanation of the old and rare observations by Wagner[139] and Bezold[17] that cardiac inhibition followed stimulation of the cervical sympathetic cord. Regardless of any anatomic dislocation of fibers from one division into another, the inherent physiologic chemical identity of each type of fiber is retained. The fibers to sweat glands, for instance, are an example of sympathetic neurons whose postganglionic nerve endings have a cholinergic action.

Both chemicals, adrenalin (including sympathin) and acetylcholine, can exert a universal or mass effect: acetylcholine through the parasympathetics, adrenalin through the sympathetics. The likelihood or danger of an excessive accumulation or release in the body of either substance is nicely counterbalanced by the ease and rapidity with which each chemical is rendered inactive or destroyed by the tissues and the blood. The quantity of these chemicals is thus kept within bounds and their influences restricted, it seems, to the mediation and transmission of nerve impulses at the effector organs.

Mass Action of the Autonomic Nervous System

The configuration of the anatomic elements and the general physiologic characteristics of the vegetative nervous system are in harmony with and indeed help support the concept of a mass action by which this system functions. The activity of the autonomics, constant, uninterrupted, generalized, and aroused to greater vigor when the body is confronted by a sudden emergency, may be ascribed chiefly to the following factors.

First, the ceaseless stream of impulses in the autonomics is translated almost at once into peripheral and general manifestations. This speaks strongly for a neurogenic rather than a hormonal reaction. Were the latter the case, more time would elapse before the effect, achieved through the intervention of the circulation, appeared; the larger the animal, the greater the interval of time. The total effect of the normal, constant, "tonic" *autonomic discharge* is to confer upon the body a *coordinated* dynamic equilibrium maintained at an optimal standard. Without this coordination the multitudinous and complex reactions of the autonomic *nervous system* would become incongruous and a kaleidoscopic helter-skelter. Claude Bernard[2] envisioned this with the insight of genius. According to him, the *coordinated*, *harmonious equilibrium* of the body is the expression of an adjusted and balanced *internal* environment, and he considered the constancy of this internal milieu a fundamental prerequisite to a free and independent existence: "la fixité du milieu intérieur est la condition de la vie libre."

An extremely interesting exposition of the biologic adaptations of bodily temperature in vertebrates and invertebrates was set forth at considerable length as far back as 1802 by Treviranus.

Second, the autonomic innervations, as a consequence of this functional dynamic state, are primed to react, when called upon, on a large scale and not piecemeal, in this way vital forces are quickly and fully *marshalled to hold off* the threat of catastrophe or annihilation Starting at levels already raised, the animal, if necessary, will attain a higher degree of quantitative responses almost instantaneously For example a normal blood sugar level of, let us say, 120 mg per 100 cc or a normal blood pressure plateau of 130/70 will mount respectively to perhaps 200 mg of sugar, and to 200 systolic blood pressure in considerably less time than if these figures to start with were well under the normal level At these new high levels, quickly reached, he is better armed to combat any sudden onslaught, i e , emergency

A Participation of Central Representations

The central ramifications of the autonomic system in the brain contribute greatly to regulating the normal dynamic balance of the vegetative functions and they also play a significant role in bringing about sudden violent states of autonomic hyperactivity * It is generally held that these various functioning elements act in a coordinated and integrated manner Marburg [9] however believed that the autonomic representations in the brain act by coordination rather than by integration By this he implied that each suprasegmental and brain stem level is an autonomic unit per se and the combined actions of multiple levels are summated and not interlocked or integrated Be this as it may the significant fact for the clinician is that the clinical expressions of generalized autonomic activity take a variety of clinical forms Common to all these clinical forms is a generalized autonomic mass reaction This is illustrated by *the cases* described in Chapter II

Emergency Function of the Autonomic Nervous System

To meet a threat of sudden disaster for instance as in combat the animal falls back upon physiologic reserves quickly mobilized by both divisions of the autonomic system (Cannon [7, 28]) Each division, differently equipped has its own type of response

The full significance of these separated yet coordinated activities of both autonomic divisions has not yet been fully appreciated by the practicing physician Many explosive" conditions such as a sudden cerebral or coronary thrombosis or an acute perforation of an intra abdominal viscus, are ushered in with a pattern of manifestations which corresponds to the picture associated with a sudden generalized sympathetic discharge cholinergic *reactions are not*

* A striking form of a central autonomic discharge is the so called diencephalic autonomic seizure carefully described by Penfield [102] The reaction was observed for instance in a woman of 41 who had periodic headaches and loss of consciousness An *aura was quickly fol*lowed by sudden vasomotor and pupillary changes lacrimation excessive sweating and salivation and often by loss of consciousness gastro intestinal manifestations were absent

lacking and may even be predominant or the adrenergic features may be to the fore

Generally speaking the clinical application of drugs and therapy in connection with these sudden disasters has centered mainly upon the degree and extent of the somatic damage sustained and an adequate appraisal of the significance of the associated autonomic disturbances has often been lacking But these disturbances may demand management long before sequelae of the somatic damage ensue and often when somatic alterations are absent The following case illustrates this point

A man A N 63 years old with no previous known episode of heart illness was suddenly and unexpectedly stricken while walking in the street with acute coronary occlusion accompanied by intense precordial pain and shock The feature of shock with its attendant aspects of cold gray skin generalized profuse sweating prostration and soon after marked hypotension dominated the picture He died the next day conscious and clear-eyed with no signs of circulatory failure This is an example of a profound autonomic hyperactivity chiefly depressor in character the patient succumbing before the train of events contingent upon the somatic injury (of the heart muscle) could develop The emphasis of therapy in this type of situation should be on bringing prompt aid to the greatly disturbed autonomic nervous system the somatic damage requiring at this stage little attention

ACTION OF THE SYMPATHETIC DIVISION

The sympathetic division by virtue of its particular autonomic design is able to set off a characteristic group of activities diffuse and wide flung In the face of a danger menacing the stability or integrity of the internal environment (equilibrium) the blood pressure almost instantly leaps to a new level the heart quickens the bowels are inhibited sugar is withdrawn from stored supplies oxygen consumption is increased the eyes are wide open the skin is moist and resilient the hairs of fur bearing animals become erect emotionally the animal is aroused and combative His reserves tapped his forces marshalled the animal is arrayed in a newly won armamentarium This he acquires as the result of the burst of activity of his entire sympathetic division aided by an augmented outpouring of adrenalin caused by stimulation of his adrenal glands through preganglionic fiber paths

Of much interest are the observations of Cannon et al [31] on cats and dogs whose sympathetic ganglia had been removed Unable to set off a sympathico adrenal reaction to meet a sudden emergency such animals especially cats nevertheless exhibit under undisturbed conditions rather well adjusted adrenergic manifestations for example blood pressure and heart rate are held up to a normal level Since the normal nervous (preganglionic) control of the adrenal glands will be lacking in such animals we must account for the sustained level of adrenergic activity by assuming that adrenalin or its allied product sympathin is still elaborated in adequate quantity in the surviving adrenergic neurons and at nerve endings The denervated adrenals may still be able to secrete

adrenalin, but its delivery to the body is ineffective (Ciminata[31]) However, animals especially cats, lacking a sympathetic nervous system cannot respond to new or unusual demands In other words under sheltered conditions the adrenergic reactions are still maintained and rather adequately, but in states of emergency these reactions cannot be made to display a range above their "quiet" levels It would appear, therefore, as if the adrenal glands may be a reservoir tapped when a sudden, urgent generalized sympathico adrenal response is provoked Throughout this upheaval, the other division of the autonomic system takes a subordinate and less spectacular, but none the less important part

Role of the Parasympathetic Division

This division, the parasympathetic, is fundamentally "protective" or "conservative," in character (Cannon [1]) Comprising the major portion of this division the vagus nerve, an ancient cardiogastric nerve and in higher phyla also a pneumogastric nerve retains its primary conservative and guardian watchfulness over respiration, circulation and digestion The parasympathetic *fibers running in the third seventh and ninth cranial nerves and in the sacral* outflow subserve a similar guardian role over the structures they innervate By virtue of this supervisory function of the parasympathetics as a whole the animal enters the "fray," i e, meets a sudden emergency, with his respiration, alimentary tract, and circulation disturbed comparatively little Moreover, when and if the parasympathetic division is provoked or stimulated by an abnormal burst of activity this division may be called upon to produce a fractional rather than a universal response The parasympathetics therefore, are likely to be responsible for an abnormally heightened reaction in but one organ or one system The absence of an integrated and universal response is quite characteristic and in keeping with the restricted anatomic distribution of the short postganglionic fibers of this division Were this division to react to its fullest potentiality it would only cause as Bard [6] has put it "responses that are not bound by physiological bonds of integration" However it must not be supposed that the parasympathetic division is incapable of producing wide spread reactions which simultaneously involve many systems of the body

Antagonism Between the Autonomic Divisions

The unfailing stream of tonic discharge the mass action of the entire autonomic system and its capacity to evoke increased quantitative reactions are supposed to depend upon the interaction of counterpoised, antagonistic autonomic forces *Exemplified as physiologic reactions in each division of the autonomic system* these forces are easily identified as normal responses in the living body and are produced readily under experimental conditions

Whereas the vitality and the potential "volatility" of the sympathetic division are well recognized, the parasympathetic system designated in a general

way as guardian and protective should not be looked upon as a passive or lethargic apparatus Quite the contrary it may be quickly whipped into action inducing bodily changes which in the main appear to be antipodal or better antagonistic to those which characterize the sympathetic division

This antagonism is observed in a number of examples The parasympathetic fibers in the third cranial nerve constrict the pupil of the eye while the sympathetic innervation contrives to keep the pupil widely dilated These opposed influences keep the pupil neither too constricted nor too dilated and what is equally important the pupil will react promptly in either direction between the poles of these opposite influences A similar dynamic state is achieved by the opposition between the parasympathetic inhibitors and the sympathetic cardiac accelerator nerves to the heart and by the augmentor parasympathetic nerves to the gastro-intestinal musculature pitted as it were against the action of the inhibitory fibers in sympathetic nerve When as in the case of the coronary vessels vasoconstriction is accomplished through the parasympathetic nerves and vasodilatation through the sympathetics the principle of opposed or antagonistic physiologic reactions is also in force

The result in all these instances is a dynamic labile state regardless of the organ or structure in question iris heart gut musculature coronary or pulmonary vessels etc This fundamental principle of balanced or *counterpoised* physiologic reactions is exemplified even in those parts of the body where only one autonomic division seems to exist Thus the smaller *peripheral blood* vessels the sweat glands and the erector pili muscles are able to undergo a dual set of antipodal reactions by means of an increase or diminution of sympathetic influences transmitted along sympathetic nerves *The* splanchnic blood vessels appear to operate on a similar principle (Tomb [iii])

Mutual Cooperation or Synergism of the Autonomic Divisions

Although the divisional forces in the autonomics *often work* in opposition to each other the body is not at the capricious mercy of these antipodal activities Rather a cooperation or mutuality of the *autonomics as a whole* underlies all the coordinated intrabodily functions both in the smooth efficiency with respect to each organ or system of organs and *with respect* to the general integration of all important bodily processes The duality of *functions* of the autonomic nervous system has therefore a stronger complemental than anticomplemental character

This advantage to the body of a dynamic equilibrium cannot be over estimated and toward the production and *maintenance* of the equilibrium both divisions of the autonomic nervous *system contribute* a vital part Accordingly the end result—a dynamic equilibrium—represents a fundamental, constructive achievement and this notwithstanding any antagonistic reactions set up in any portions of the autonomic system itself

The role of a double and antagonistic innervation has many exceptions and

a cooperative duality in the autonomic system can be discerned even in a single division For example, in some of the peripheral effectors supplied by the sympathetics, i e, the cutaneous blood vessels vasoconstriction and vasodilatation are accomplished apparently without parasympathetic nerves

In addition to local or peripheral examples, the principle of synergistic or mutual cooperation of the vegetative nervous system is witnessed in a single division of the autonomics, here, however, the action affects simultaneously more than one system of blood vessels, e g, cutaneous blood vessels and those within the abdominal cavity, or cutaneous and coronary vessels In the case of the cutaneous vessels, a viscero or splanchnocutaneous reflex is established During the ejection of blood from the cutaneous vessels, following sympathetic vasoconstriction, the splanchnic vessels in the abdomen become filled as a result of vasodilatation The dilatation is probably also of sympathetic origin Similarly, when under certain circumstances the cutaneous vascular bed is constricted and emptied of blood the coronary vessels of the heart, as a result of sympathetic vasodilatation, will widen and up to a point enable the heart to secure an increased quantity of blood These anatomic and functional relationships represent a synergistic or cooperative regulation which may be and often is protective and life saving

The ease with which the activity of the sympathetic division becomes ascendant during emergency states is noteworthy This is due not only to an increased stimulation or burst of activity on the part of the sympathetics, but in some measure to a supplemental parasympathetic cooperation accomplished by diminishing the tonus of those parts of the body innervated by the parasympathetics, an augmentated tonic sympathetic effect is thus achieved

Pharmacologic attributes and responses of each autonomic division also point to a mutuality or cooperation of both divisions The reaction on the parasympathetic division induced by atropine may closely resemble the effects of adrenalin on the sympathetic division Dilatation of the pupil, an accelerated heart rate and inhibition of peristalsis are pharmacologic responses which may be common to each autonomic division Again certain drugs are amphotropic (Pick [101], Danielopolu [41]) possessing an almost equal influence on both divisions

Coordination and Integration of Central Autonomic Functions

The vast and complicated autonomic regulations in the body are accomplished by segmental reactions involving reflexes mediated at spinal cord level, and by activities which are controlled for the most part if not entirely at higher levels

The higher representations comprise anatomic and physiologic elements of both autonomic divisions These elements are also coordinated and integrated with others which govern somatic functions The overlapping or intermingling of autonomic and somatic representations exists throughout the entire motor

cortex and probably in the sensory cortical territory also in the thalamic and striatal levels and less extensively, in the hypothalamus

The patterns of reaction of the various levels of autonomic representation of the brain are not identical For example the group of effects set off at the hypothalamus is predominantly adrenergic and that at the medulla cholinergic This differentiation with respect to brain levels may be observed in the clinical picture of hyperinsulinism In man four clinical stages develop and each stage is claimed to be related to the total brain substance depressed and to the territory released from the influence of higher centers and rendered predominant or hyperactive

The levels of central autonomic functions in connection with the level of blood sugar and in relation to anoxia and the oxidation of carbohydrates have been studied by Gellhorn[55] and Himwich[56]

BIBLIOGRAPHY

[1] ANDERSON H K The paralysis of involuntary muscle II On the action of pilocarpine physostigmine and atropine on the paralyzed iris J Physiol 1905 *33* 414

[2] ANREP G V AND SEGALL H N The regulation of the coronary circulation Heart 1926 *13* 239

[3] BACQ Z M La pharmacologie du système nerveux autonome et particulièrement du sympathique d après la théorie neurohumorale Ann d physiol 1934 *10* 46

BAEHR C AND PICK E I Pharmakologische Studien an der Bronchialmuskulatur der überlebenden Meerschweinchenlunge Arch f exper Path u Pharmakol 1913 *74* 41

[5] BARBOUR H G Die Struktur verschiedener Abschnitte des Arteriensystems in Beziehung auf ihr Verhalten zum Adrenalin Arch f exper Path u Pharmakol 1912 *68* 41

[6] BARD P In MacLeod J J R Physiology in modern medicine St Louis Mosby 1941

BEATTIE J BROW G R AND LONG C N H The hypothalamus and the sympathetic nervous system Part One The dependence of the extrasystolic arrhythmia of the heart produced by chloroform upon the integrity of the sympathetic nervous system and the use of this arrhythmia as an indicator of sympathetic activity Res Publ Ass nerv ment Dis 1930 *9* 249

BEATTIE J BROW G R AND LONG C N H The hypothalamus and the sympathetic nervous system Part Two The higher connections of the sympathetic nervous system as studied by experimental lesions of the hypothalamus Res Publ Ass nerv ment Dis 1930 9 294

BEATTIE J BROW G R AND LONG C N H Physiological and anatomical evidence for the existence of nerve tracts connecting the hypothalamus with spinal sympathetic centers Proc Roy Soc Series B 1930 *106* 253

[8] BENDER M B Fright and drug contractions in denervated and ocular muscles of monkeys Am J Physiol 1938 *121* 609

BENDER M B Sensitized pupillary dilator and facial muscles as indicators of sympathetic and parasympathetic substances in blood Proc Soc Exper Biol & Med 1938 39 62

BERNARD C Influence du grand sympathique sur la sensibilité et sur la calorification Compt rend Soc de biol 1851 2 163

[11] BERNARD C Recherches expérimentales sur le grand sympathique et spécialement sur l influence que la section de ce nerf exerce sur la chaleur animale Compt rend Soc de biol 1853 5 77

[12] BERNARD C Leçons sur la physiologie du système nerveux Paris Baillière 1858

[15] BERNARD C Du rôle des actions réflexes paralysantes J de l anat et de la physiol 1861 *1* 507

[16] BERNARD C Leçons sur les phénomènes de la vie commune aux animaux et aux végétaux Paris Baillière 1878

[17] BERRY J L BRAILSFORD J F AND DE BURGH DALY I The bronchial vascular system in the dog Proc Roy Soc Series B 1931 *109* 214

[17a] BEZOLD In Tigerstedt R *Physiologie des Kreislaufes Berlin de Gruyter 1921 23*

[18] BIDDER F H AND VOLKMANN A W Die Selbstandigkeit des sympathischen Nerven systems *durch anatomische Untersuchungen nachgewiesen Leipzig Breitkopf & Hartel* 1842

[19] BILLINGSLEY P R AND RANSON, S W *On the number of nerve cells in the ganglion cervicale superius and of nerve fibres in the cephalic end of the truncus sympathicus in the* cat and on the numerical relations of the preganglionic and postganglionic neurones J Comp Neurol 1918 *29* 359

[20] *BRADFORD J R AND DEAN H P On the innervation of the pulmonary vessels Proc* Physiol Soc Feb 9 1889 In *J Physiol 1889 10*

[21] BRADFORD J R AND DEAN, H P The innervation of the pulmonary vessels Proc Roy *Soc Series B 1889 45 369*

[22] BRADFORD J R AND DEAN H P The pulmonary circulation *J Physiol 1894 16 34*

[23] BRESLAUER V Die Pathogenese der trophischen Gewebeschäden nach Nervenverletzung *Deutsche Ztschr f Chir 1919 150 50*

[24] BRODIE T G AND DIXON W E Contributions to the physiology of lungs II On the innervation of the pulmonary blood vessels and some observations on the action of suprarenal extract *J Physiol 1904 30 476*

[25] BRUCE A N Ueber die Beziehung der sensiblen Nervenendigungen zum Entzundungsvorgang Ztschr f exper Path u Pharmakol *1910 63 424*

[26] CAMPBELL J A The effects of certain animal extracts upon the blood vessels *Quart J* Exper Physiol 1911 *4* 1

[27] CANNON W B Physiological regulation of normal states some tentative postulates concerning biological homeostasis In À Charles Richet p 91 Paris *1926*

[28] CANNON W B The sympathetic division of the autonomic system in relation to homeostasis Res Publ Ass nerv ment Dis 1930 *9* 181

[29] CANNON W B Studies on the conditions of activities in endocrine organs XXVI A hormone produced by sympathetic action on smooth muscle Am J Physiol 1931 *96* 392

[30] CANNON W B AND LISSAK K *Evidence for adrenaline in adrenergic neurones* Am J Physiol 1939 *125* 765

[31] CANNON W B NEWTON H F BRIGHT E M MENKIN V AND MOORE R M Some aspects of the physiology of animals surviving complete exclusion of sympathetic nerve impulses Am J Physiol 1929 *89* 84

[32] CANNON W B AND ROSENBLUETH A Sympathin E and sympathin I Am J Physiol 1933 *104* 557

[33] CANNON W B AND ROSENBLUETH A Autonomic neuro effector systems New York Macmillan 1937

[34] CIMINATA A Ueber Nebennierenentnervung und ihre *Folgen fur den Organismus* Arb a d neurol Inst a d Wien Univ *1926* 8 95

[35] COFFEY W B BROWN P K AND HUMBER J D Angina pectoris The anatomy physiology and surgical treatment *New Orleans Dickerson 1927*

[36] CYBULSKI N Ueber die Funktion der Nebenniere *Gazeta lekarska (Warsaw) 1895 12* 299

* CYBULSKI N Weitere Untersuchungen uber die Funktion der Nebenniere Bull int Acad Cracovie 1895
DALE H H Chemical transmission of the effects of nerve impulses Brit M J 1934 *1* 835
* DALE H H Transmission of nervous effects by acetylcholine Bull New York Acad Med 1937 *13* 379
* DALE H H AND FELDBERG W The chemical transmitter of nervous stimuli to the sweat glands of the cat J Physiol 1934 *81* 40
* DANIÉLOPOLU D Les trois lois fondamentales qui régissent le fonctionnement du système nerveux végétatif à l'état normal et pathologique Bull et mém Soc méd d hop de Bucarest 1928 *10* 137 Also in Klin Wchnschr 1928 *7* 1748
* DE BURGH DALY I Reactions of the pulmonary and bronchial blood vessels Physiol Rev 1933 *13* 149
DE BURGH DALY I The physiology of the bronchial vascular system Harvey Lect 1936 *31* 235
* DE BURGH DALY I AND VON EULER U The functional activity of the vasomotor nerves to the lungs Proc Roy Soc Series B 1932 *110* 92
DE NÓ L Acetylcholine in superior cervical sympathetic ganglion Am J Physiol 1938 *121* 331
* DIXON W E AND HOYLE J C Studies in the pulmonary circulation I The vasomotor supply J Physiol 1928 *65* 299
* DIXON W E AND HOYLE J C Studies in the pulmonary circulation II The action of adrenaline and nicotine J Physiol 1929 *67* 77
* DIXON W E AND HOYLE J C Studies in the pulmonary circulation III The action of histamine J Physiol 1930 *70* 1
* DOI Y On the existence of antidromic fibers in the frog and their influence on the capillaries J Physiol 1920 *34* 227
DUNBAR H F Emotions and bodily changes New York Columbia Univ Press 1935
* ECKARDT P Zur Frage pulmocoronarer Reflexe bei Lungenembolie Pflügers Arch 1938 *241* 224
ELLIOTT T R The action of adrenalin J Physiol 1905 *3* 401
ERIKSON E Zur Kenntnis des kleinen Kreislaufes bei der Katze Skandin Arch f Physiol 1907 *19* 46
VON EULER U S A vaso-constrictor action of acetylcholine on the rabbit's pulmonary circulation J Physiol 1932 *74* 271
* FRANÇOIS FRANCK C A Nouvelles recherches sur l action vaso-constrictive pulmonaire du grand sympathique Arch de physiol 1895 *7* 744 816
* FUHNER H AND STARLING E H Experiments on the pulmonary circulation J Physiol 1913 *47* 286
* GELLHORN E Fundamental principles in the adjustment reactions of the organisms of anoxia Ann Int Med 1941 *14* 1518
* Gerhardt D Ueber die Wirkungsweise der blutdrucksteigernden Substanz der Nebennieren Arch f exper Path u Pharmakol 1900 *44* 161
* GOLLWITZER MEIER K KRAMER K AND KRUGER E Die Wirkung des Adrenalins auf die Energetik des Herzen Pflugers Arch 1936 *237* 639
* GOLLWITZER MEIER K AND KRUGER E Einfluss der Herznerven auf den Gaswechsel des Warmblutherzens Pflügers Arch 1938 *240* 89
* GREENE C W An analysis of the efferent pathways and vasomotor control of the coronary circulation of the dog Am J Physiol 1931 *97* 526
* GREENE C W The nerve control of the coronary vessels with new experimental evidence for the pathways of efferent constrictor and dilator neurones in the dog Am J Physiol 1935 *113* 361

15 Bernard C Du rôle des actions réflexes paralysantes J de l anat et de la physiol 1864 *1* 507
16 Bernard C Leçons sur les phénomènes de la vie commune aux animaux et aux végétaux Paris Baillière 1878
17 Berry J L Brailsford J F and De Burgh Daly I The bronchial vascular system in the dog Proc Roy Soc Series B 1931 *109* 214
1 a Bezold In Tigerstedt R Physiologie des Kreislaufes Berlin de Gruyter 1921-23
18 Bidder F H and Volkmann A W Die Selbstandigkeit des sympathischen Nervensystems durch anatomische Untersuchungen nachgewiesen Leipzig Breitkopf & Hartel 1842
19 Billingsley P R and Ranson S W On the number of nerve cells in the ganglion cervicale superius and of nerve fibres in the cephalic end of the truncus sympathicus in the cat and on the numerical relations of the preganglionic and postganglionic neurones J Comp Neurol 1918 *29* 359
20 Bradford J R and Dean H P On the innervation of the pulmonary vessel Proc Physiol Soc Feb 9 1889 In J Physiol 1889 *10*
21 Bradford J R and Dean H P The innervation of the pulmonary vessels Proc Roy Soc Series B 1889 *45* 369
22 Bradford J R and Dean H P The pulmonary circulation J Physiol 1894 *16* 34
23 Breslauer V *Die Pathogenese der tropischen Gewebeschaden nach Nervenverletzung* Deutsche Ztschr f Chir 1919 *150* 50
24 Brodie T G and Dixon W E Contributions to the physiology of lungs II On the innervation of the pulmonary blood vessels and some observations on the action of suprarenal extract J Physiol 1904 *30* 476
25 Bruce A N Ueber die Beziehung der sensiblen Nervenendigungen zum Entzundungsvorgang Ztschr f exper Path u Pharmakol 1910 *63* 424
26 Campbell J A The effects of certain animal extracts upon the blood vessel Quart J Exper Physiol 1911 *4* 1
27 Cannon W B Physiological regulation of normal states some tentative postulates concerning biological homeostasis In A Charles Richet p 91 Paris 1926
28 Cannon W B The sympathetic division of the autonomic system in relation to homeostasis Res Pbl Ass nerv ment Dis 1930 *9* 181
29 Cannon W B Studies on the conditions of activities in endocrine organs XXVI A hormone produced by sympathetic action on smooth muscle Am J Physiol 1931 *96* 392
30 Cannon W B and Lissák R Evidence for adrenaline in adrenergic neurones Am J Physiol 1939 *125* 765
31 Cannon W B Newton H F Bright E M Menkin V and Moore R M Some aspects of the physiology of animals surviving complete exclusion of sympathetic nerve impulses Am J Physiol 1929 *89* 84
32 Cannon W B and Rosenblueth A Sympathin E and sympathin I Am J Physiol 1933 *104* 557
33 Cannon W B and Rosenblueth A *Autonomic neuro effector system* New York Macmillan 1937
34 Ciminata A Ueber Nebennierenentnervung und ihre Folgen fur den Organismus Arb a d neurol Inst a d Wien Univ 1926 *28* 95
35 Coffey W B Brown P K and Humber J D Angina pectoris The anatomy physiology and surgical treatment New Orleans Dickerson 1927
36 Cybulski N Ueber die Funktion der Nebenniere *Gazeta lekarska (Warsaw)* 1895 *17* 299

86 LeBlanc, C and van Wyngaarden C de L. Innervation der Lungengefasse Pflügers Arch 1924 *204* 601
87 Lewis T Vascular disorders of the limbs New York Macmillan 1936
88 Lichtwitz L Ueber Wanderung des Adrenalins in Nerven Arch f exper Path u Pharmakol 1908 *58* 221
89 Livingston W K The clinical aspects of visceral neurology p 35 Springfield Ill Thomas 1935
90 Loewi O Ueber humorale Uebertragbarkeit der Herznervenwirkung Pflüger's Arch 1921 *189* 239
91 Löhr H Untersuchungen zur Physiologie und Pharmakologie der Lunge Ztschr f d ges exper Med 1924 *39* 67
92 Marburg O Ueber die neueren Fortschritte in der topischen Diagnostik des Pons und der Oblongata Deutsche Ztschr f Nervenh 1911 *41* 41
93 Marine D Studies on the pathological physiology of the exophthalmos of Graves disease Ann Int Med 1938 *12* 443
94 Marine D Does the study of experimental exophthalmos offer any clue to the fundamental nature of Graves disease? International Goiter Conference (3rd) 1938 Transactions p 7
95 Marine D and Rosen S H The exophthalmos of Graves disease Its experimental production and significance Am J M Sc 1934 *188* 565
96 McDowall, R J S The control of the circulation of the blood London Longmans Green 1938
97 McGregor H G The emotional factor in visceral disease London Milford 1939
Meyer O B Ueber einige Eigenschaften der Gefassmuskulatur mit besonderer Berücksichtigung der Adrenalinwirkung Ztschr f Biol 1906 *48* 352
98 Miller H R and Taub H Exophthalmos in rabbits produced by oxyquinoline sulphate Proc Soc Exper Biol & Med 1935 *3* 1207
99 Moller S Kritisch experimentelle Beiträge zur Wirkung des Nebennierenextraktes (Adrenalin) Therap Monatschr 1905 *19* 54 672 1906 *20* 25
100 Nachmansohn D La transmission de l'influx nerveux dans le système nerveux central Compt rend Soc de biol 1937 *126* 783
101 Penfield W G Diencephalic autonomic epilepsy Arch Neurol & Psychiat 1929 *22* 358
102 Petitjean G Action de quelques médicaments vaso-moteurs (nitrite d'amyle adrénaline ergot de seigle) sur la circulation pulmonaire J de physiol et de path gén 1908 *10* 403
103 Pick E P Pharmakologie des vegetativen Nervensystems Deutsche Ztschr f Nervenh 1928 *106* 238
104 Pilcher J D and Sollmann T Studies on the vasomotor center III The action of epinephrin J Pharmacol & Exper Therap 1915 *6* 339
105 Plumier L La circulation pulmonaire chez le chien Arch internat de physiol 1904 *1* 176
106 Plumier L Action de l'adrénaline sur la circulation cardio-pulmonaire J de physiol et de path gén 1904 *6* 665
Plumier L Action de la trinitrine et du nitrite d'amyle sur la circulation cardio-pulmonaire J de physiol et de path gén 1905 *7* 596
Plumier L Action du nitrite d'amyle sur la circulation pulmonaire Compt rend Soc de biol 1906 *60* 282
Prevost J L and Saloz J Contribution à l'étude des muscles bronchiques Arch internat de physiol 1909 *8* 326
Rein H Die Physiologie der Herz Kranzgefasse Ztschr f Biol 1931–32 *9* 101
107 Richardson E P and White P D Sympathectomy in the treatment of angina

[61] GREENE C W Control of coronary blood flow by reflexes arising in widely distributed regions of the body Am J Physiol 1935 *113* 299
[62] GREENE C W An analysis of the relations of coronary constrictor and dilator nerves in the cervical vagosympathetic of the dog Am Heart J *1936 11* 592
[63] HEGER P AND PHILIPPSON M Adrénaline et circulation pulmonaire Bull Acad roy de méd de Belgique 1912 *26* 335
[64] HENRIQUES V Untersuchungen über den Einfluss des Nervensystems auf den respiratorischen Stoffwechsel der Lungen Skandin Arch f Physiol 1893 *4* 194
[65] HEYMANS J F AND VERCOULLIE J L adrénaline agit sur la petite comme sur la grande *circulation In Mélanges biologiques livre dédié à Ch Richet* p *199* Paris Impr de la Cour d appel 1912
[66] HIMWICH H E MARTIN S J ALEXANDER F A D AND FAZEKAS J F EKG changes during hypoglycemia and anoxemia (cortical depression and autonomic release) Endocrinology 1939 *24* 536
[67] HINRICHSEN J AND IVY A C Effect of stimulation of visceral nerves on coronary blood flow in dogs Arch Int Med *1933 51 932*
[68] HIRAKAWA K A study of the contracting and dilating apparatus of the pulmonary blood vessels Acta scholae med univ imp in Kioto 1925 *7* 467
[69] HOCHREIN M AND KELLER J Untersuchungen am Koronarsystem Arch f exper Path u Pharmakol 1931 *159* 300
[70] HOFF F Vegetatives Nervensystem und innere Sekretion In Lehrbuch der speziellen pathologischen Physiologie Jena Fischer 1935
[71] HOVELACQUE A Anatomie des nerfs craniens et rachidiens et du système grand sympathique chez l homme Paris Doin 1927
[72] HRYNTSCHAK T AND SPIEGEL E A Ueber den Mechanismus der automatischen Blase Klin Wchnschr 1924 *40* 1819
[73] JELLIFFE S L Discussion of Cannon s The sympathetic division of the autonomic nervous system in relation to homeostasis Res Publ Ass nerv ment Dis 1930 *9* 194
[a] KATZ L N AND JOCHIM K Observations on the innervation of the coronary vessel of the dog Am J Physiol 1939 *126* 395
[74] KENNARD M The cortical influence on the autonomic nervous system In Handbuch der Neurologie (Bumke & Foerster) II 476 Berlin Springer 1937
[75] KERR H H Surgical treatment of angina pectoris Ann Clin Med 1925 *4* 30
[76] KERR H H Operative treatment of angina pectoris Ann Surg 1925 *82* 354
[77] KOLM R AND PICK E P Ueber das Vasomotorenzentrum des Kaltbluters Arch f exper Path u Pharmakol 1920 *87* 135
[78] KRAWKOW N P Ueber die Wirkung von Giften auf die Gefasse isolierter Fischkiemen *Pflugers Arch 1913 151* 583
[79] KUNTZ A The autonomic nervous system p 500 Philadelphia Lea & Febiger 1934
[80] KURÉ K Ueber den Spinalparasympathikus Basel Schwabe 1931
[81] KURÉ K Spinalparasympathikus und Kreislauf Cardiologia 1937 *1* 95
[82] KURE K ICHIKO K I AND ISHIKAWA K On spinal parasympathetic Physiological significance of spinal parasympathetic system in relation to digestive tract Quart J Exper Physiol 1931 *21* 1
[83] KURÉ K NITTA Y TSUJI M SHIRAISHI K AND SUENOGA B Die histologische Darstellung der parasympathischen Fasern in den hintern Rückenmarkswurzeln der Lumbalsegmente Pfluger s Arch 1928 *218* 573
[84] LANGENDORFF O Ueber die Innervation der Koronargefasse Zentralbl f Physiol 1907 *21* 551
[85] LANGLEY J N AND ANDERSON H K On reflex action from sympathetic ganglia J Physiol 1894 *16* 410

Wernøe T B Viscero-cutane Reflexe Pflügers Arch 1925 *210* 1
White J C The autonomic nervous system New York Macmillan 1935
Wiggers C J The action of adrenalin on the pulmonary circulation J Pharmacol & Exper Therap 1909 *1* 341
Wiggers C J In Diseases of the coronary arteries and cardiac pain E F Ey R Levy New York Macmillan 1936
Wittkower F Einfluss der Gemütsbewegungen auf den Korper Wien Sensen Verlag 1936
Wood H C A physiological study of the pulmonary circulation Am J Physiol 1902 *6* 283
Wood H C The vaso motor supply of the lungs J Pharmacol & Exper Therap 1910 *2* 394
Wood H C Studies on the pulmonary circulation J Exper Med 1911 *14* 326
Woollard H H Innervation of the heart J Anat 1926 *60* 345

pectoris Comparison with those from paravertebral alcohol injection Am J M Sc 1929 *177* 161

113 RJASANSKIJ A Zur Anteilnahme des Vagus und Sympathicus in der Innervation der Lungen J sovrem Chir 1928 *3* 1023 Abstracted in Ber u d ges Biol Abt B 1929 30 *52* 267

114 ROMM S O Die Wirkung der gefassverengenden und gefasserweiternden Substanzen auf die Lungenkreislaufsdauer des Blutes Pflüger s Arch 1924 *204* 668

115 ROSENOW G Hirnstichleukocytose Untersuchungen über die zentralvegetative Blutregulation Ztschr f d ges exper Med 1929 *64* 452

116 SCHAFER E S AND LIM R K S The effects of adrenaline on the pulmonary circulation Quart J Exper Physiol 1919 *12* 157

117 SCHERF D AND SCHONBRUNNER E Ueber Herzbefunde bei Lungenembolien Ztschr f klin Med 1935 *128* 455

118 SCHERF D AND SCHONBRUNNER E Ueber den pulmokoronaren Reflex bei Lungenembolien Klin Wchnschr 1937 *16* 340

119 SCHLESINGER R Ueber die Wirkung einiger lokaler Anästhetika auf die Lungengefässe Arch f exper Path u Pharmakol 1931 *160* 479

120 SCHMITT W Untersuchungen zur Physiologie der Plazentargefasse Ztschr f Biol 1922 *75* 19

121 SCHMITT W Ueber den Einfluss der Wasserstoffionenkonzentration auf die Gefasse der menschlichen Placenta Ztschr f Biol 1923 *79* 45

122 *SMITH H W The physiology of the kidney New York Oxford Univ Press 1937*

123 SOKOWNIN M In Kowalewsky N and Arnstein C Bericht uber die physiologischen und histologischen Mitteilungen der 4 Versammlung russicher Naturforscher *Pfluger s Arch 1874 8* 596

124 SPERANSKAJA STEPANOWA E N Zur Physiologie der Hautdrusen des Frosches I Sekretorische und hemmende Nerven der Froschhautdrüsen Pflüger s Arch 1925 *209* 1

125 SPERANSKAJA STEPANOWA E N Zur Physiologie der Hautdrüsen des Frosches II Rolle des peripheren Neurons bei der Sekretion der Hautdrüsen Pfluger s Arch 1925 *209* 22

126 STIEGEL F A Die Zentren des autonomen Nervensystems Berlin Springer 1928

127 STRUEFF N Zur Frage der bakteriellen Lungenembolie Virchow s Arch 1909 *198* 211

128 SZYMONOWICZ L Die Funktion der Nebenniere Pflüger s Arch 1896 *64* 97

129 TESTUT L Traité d anatomie humaine Paris Doin 1928

130 TIGERSTEDT R Physiologie des Kreislaufes Berlin de Gruyter 1921–23

131 TOMB J W Shock and allied conditions Lancet 1937 *II* 1416

132 TREVIRANUS G R Biologie oder Philosophie der lebenden Natur fur Naturforscher und Aertzte Gottingen Rower 1802–22

133 *TRIBE E M Effect of adrenaline on the pulmonary circulation J Physiol 1912 45* xx

134 TRIBE E M Vasomotor nerves in the lungs J Physiol 1914 *48* 154

135 VELICH A Ueber die Einwirkung des Nebennierensaftes auf den Blutkreislauf Wien med *Bl 1896 19* 227 245 262 279 295 311 324

136 VELICH A Ueber die Einwirkung des Nebennierenextractes auf den Blutkreislauf Wien med Wchnschr 1898 *48* 1258

137 VILLARET M JUSTIN BESANÇON L AND BARDIN P Physio pathologie des accidents mortels consécutifs aux embolies pulmonaires Bull et mém Soc méd d hôp de Paris 1936 *52* 936

138 VILLARET M JUSTIN BESANÇON L AND BARDIN P Recherches sur la prévention experimentale des accidents consécutifs aux embolies pulmonaires *Bull et mém Soc* méd d hôp de Paris 1936 *52* 941

139 WAGNER IN TIGERSTEDT R Physiologie des Kreislaufes Berlin de Gruyter 1921–23

140 WEBER E Ueber aktive *Aenderungen der arteriellen Blutfülle der Lungen* Arch f Anat u Physiol 1910 Supplement 377

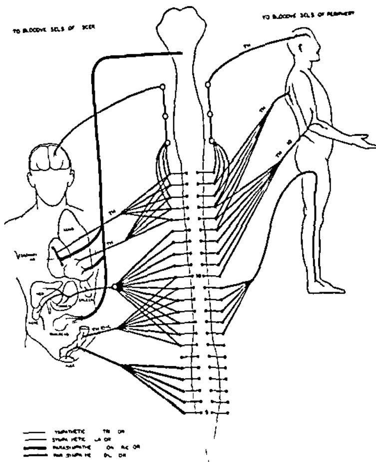


FIG 13 —Sympathetic and Parasympathetic Innervation to the Blood Vessels of the Viscera and Periphery The parasympathetic cranial outflow in man is by way of the IIIrd VIIth IXth Xth XIth cranial nerves the sacral outflow by way of S 2 3 4 To simplify the drawing the following parasympathetic fibers were omitted Dilator fibers in the VIIth cranial nerve passing via the chorda tympani nerve to vessels of the submaxillary gland dilator fibers in the IXth cranial nerve passing via the small petrosal nerve to vessels of the parotid gland also fibers passing via the lingual nerve to blood vessels of the tongue dilator fibers in the pelvic nerves nervi erigens (S 2-4) which go to the blood vessels of the penis Cephalad to the rhombencephalon efferent sympathetic neurons descend from the posterior hypothalamic area to the spinal levels It has been suggested that these neurons serve as an upper pathway for impulses arising in the cortex or diencephalon

contain muscle elements The nerves extend to the large vessels (Schretzenmayr [177, 178]) and even to the aorta (Hurthle[107]) Histologists now also admit that capillaries possess vasomotor innervations consisting of a diffuse network which

CHAPTER V

The Autonomic Regulation of Circulation

FROM the cardiac pump to the tiniest capillaries and back the circulation is governed by autonomic regulation. This regulation is accomplished largely by a nervous apparatus which is made up of central and peripheral components. Through highly organized reflex adjustments these components are coordinated to chemical, physical and mechanical processes which are also under the control of the autonomic system. Many factors contribute to the hemodynamics, e.g., arterial, capillary and venous pressures, blood velocities, cardiac rate and output, the tonicity of the vascular conduits, the quantity and quality of the blood mass, the osmotic pressure of the blood, the shunting *of circuits or tapping of blood depots. But the primary determinant in regulating* the circulation and its hemodynamics is the metabolic need of the tissues associated with the activity of external and internal respiration. Specialized chemicals and hormones—adrenalin, acetylcholine, pituitrin, histamine—have a prominent influence. So have variations in intrabodily temperature and water content, shifts in *p*H and in concentrations of minerals and electrolytes.

This galaxy of integrating processes has its anatomic representations in the neuraxis. At various levels from the telencephalon through the spinal cord regulatory devices exist; these are especially well developed in the brain stem. Of the central stations, the hypothalamus especially is dealt with in detail in this text, but the other control areas are not ignored.

To assess more accurately the significance of the central supervision of the circulation, it will be useful to consider the autonomic circulatory controls as a whole, peripheral as well as central.

Autonomic Peripheral Regulations

The peripheral regulations of the circulation are carried out by chemical, physical, mechanical and nervous activities. The latter are mediated by sympathetic and parasympathetic pathways, and by intrinsic and extrinsic reflexes. The extrinsic reflexes especially are closely bound up with metabolism and respiration. Neurohormonal influences play their part in all these processes.

A. By Sympathetic Neurons

Sympathetic efferent fibers innervate a large part of the peripheral vascular apparatus. Nerve fibrils have been demonstrated in arterial vessels whose walls

the liver will not retain excessive fluid for instance an inordinate quantity of blood reaching the liver will have its fluid constituents quickly expelled (Mautner[140]) It is interesting to note that many years ago Ikalowicz and Pal[158] and Pal[159] suspected that the liver possessed a specialized nervous regulation

Innervation and Function of the Pulmonary Circulation A generalized outburst of sympathetic activity probably entails the participation of practically all the vascular circuits in the body In all this the pulmonary circulation possesses a special interest with regard to the dynamics governing the heart and lungs in situ as a single unit and with respect to the process of ventilation Any tendency for the lungs to become overfilled with blood which is ejected out of the periphery as a result of vasoconstriction is guarded against by a synchronized vasoconstriction of the pulmonary vessels themselves A concomitant relaxation of the bronchial musculature also takes place At one and the same time therefore the danger of inundating the lesser circulation is prevented and the ventilating passages are opened more freely to permit the ingress of oxygen Touched off simultaneously as a massive discharge these adjustments of the pulmonary circulation together with those instigated in the splanchnic coronary cerebral and other circuits remain orderly and coordinated Moreover widespread and variegated as these peripheral responses are they spring in large part from the brain stem and other brain levels

The nervous regulation of the pulmonary circulation (see p 65 for innervation) seems to obey the same physiologic laws which obtain in many other circuits of the general circulation The pulmonary blood vessels undergo sympathetic constriction and parasympathetic (vagal) dilatation and these effects operate with the synchronized effect of parasympathetic constriction and sympathetic dilatation exerted upon the musculature of the bronchi and upon the coronary tributaries of the heart The lungs in reality consist of two "organs" — a ventilating apparatus and a circulatory system—and each organ is supplied by an independent group of sympathetic and parasympathetic fibers

Many clinical affections remain confined largely and almost wholly to one organ This may often be observed in emphysema silicosis tuberculosis and carcinoma where the alveoli and bronchi are primarily involved[161] However in these pulmonary diseases the dynamics of the pulmonary circulation may eventually become disturbed Conversely the pulmonary circulation may receive the brunt of the disturbance as in congenital heart disease mitral disease and so called essential pulmonary hypertension (Eppinger and Wagner[162]) the ventilating apparatus continues to function fairly well until the respiratory membrane becomes greatly altered The following case of chronic emphysema complicated by advanced pulmonary hypertension of long duration emphasizes the part played by involvement of both organs

H I 45 years old a patient in Montefiore Hospital with emphysema during the greater part of his adult life developed pulmonary hypertension as a result of marked emphysema The clinical manifestations of pulmonary hypertension marked cyanosis polycythemia and

is an extension of the sympathetic supplies (Krogh[111]) Vasoconstriction and vasodilatation are carried out by means of this network To a major degree the latter effect is also accomplished by chemicals, i e, acetylcholine, histamine, metabolites, and probably even by extremely high dilutions of adrenalin Specialized cells in the capillaries, the Rouget cells,[173, 174] were at one time considered to be delicate extensions of the autonomic nervous system, but this is now doubted The capillaries of the heart, according to Woollard,[198] show no nerve fibrils The intrinsic autonomic activity of the heart depends, however, upon a fine network of intracardiac nerve fibrils and ganglia (Hering[78])

Of the chemical substances and of the special products of metabolism which join in the regulation of blood vessels we shall have more to say presently Adrenalin which may be designated as a chemical postganglionic substance acetylcholine, histamine, pituitrin, and a host of chemophysical factors—pH concentrations of electrolytes, the quantity of CO_2, of oxygen (oxygen lack), many hormones—all help to determine the tonicity of the capillary vessels Other reactions such as the Snellen or the Loven reflexes the skin reflex (flare reaction), and the local capillary reaction to cold, also constitute regulatory devices, probably sympathetic in character, which act on the capillaries

Sympathetic Efferent Fibers to the Cardiovascular Apparatus* The sympathetic efferent supplies to various sections or districts of the cardiovascular system do not all cause identical regional reactions (Fig 18) since the functions of these nerves are not all alike Thus the cutaneous peripheral circulation receives sympathetic vasoconstrictors but it is not conclusively determined whether the vessels of the skin and muscles receive sympathetic vasodilators The splanchnic vessels have sympathetic vasoconstrictors and perhaps vasodilators (According to Dale[41, 4] stimulating the splanchnic nerves after blocking the vasoconstrictors with ergotamine, produces a drop in blood pressure which is not checked by atropine Wiggers[196] and others however, deny the existence of sympathetic splanchnic vasodilators) The coronary circulation possesses sympathetic vasodilators and similarly the hepatic veins according to Mautner[138, 139] and Bauer et al[10]

As a result of these differences in function of peripheral subdivisions of the sympathetic system a massive discharge of the entire sympathetic division is made up of a variety of local effects A large volume of blood is diverted from the skin and the skeletal musculature and out of the blood depots to supply vital organs like the brain and the heart On the other hand the musculature as a whole, the skin the lungs possibly the bone marrow and blood depot organs like the spleen are probably able to increase their capacity by virtue of nervous adjustments The blood depot organs are able to hold large quantities of blood The liver in this respect is an exception Under normal circumstances

*As a rule the impulses travel centrifugally but in efferent neurons they may sometimes be antidromic in direction (Bayliss[13])

ventilating apparatus became greatly impaired and the patient succumbed to unrelieved congestive heart failure combined with pulmonary insufficiency

The innervations and functions of the pulmonary circulation are important factors in these and other examples of cardiac and pulmonary disease

Sympathetic Cardio-Accelerator Fibers A special group of fibers the cardio-accelerator fibers (Figs 18 and 35) with cell bodies at levels Th 1 to 5 exerts an excitatory effect on the heart Stimulating these fibers produces a rise in the heart rate and an increased contraction of the auricles and ventricles Sectioning these fibers or blocking them with ergotamine for example turns the heart over to the unhampered action of the cardio-inhibitory mechanism and the heart becomes slowed

Sympathetic Hypothalamo-Spinal Fibers (Fig 41) A sympathetic efferent tract arising from the posterior hypothalamus has been identified by Beattie Brow and Long[16, 1] Descending intraspinally to the lateral horn cells the fibers of this tract continue to the stellate ganglion and thence to the cardiac plexuses Interrupting this fiber tract or destroying the posterior hypothalamic area will abolish the remarkable extrasystolic arrhythmia caused by chloroform inhalation It is now advocated that this part of the brain participates in the regulation of the cardiac rhythm (p 131) and that these hypothalamo-spinal fibers constitute an upper neuron pathway connecting with the sympathetic neurons which leave the spinal cord at the thoracic and lower levels

B By Parasympathetic Neurons

As in the case of the sympathetic division the parasympathetic is also able to discharge in a massive or generalized manner As a rule however the response is fragmentary i e restricted to one or a few regions

Absence of Parasympathetic Fibers to Peripheral Vessels The parasympathetic distribution to the cardiovascular system differs from that of the sympathetic Despite the well established vasodilator action of acetylcholine on the capillaries of the skin and in the limb these capillaries as well as others are apparently devoid of parasympathetic nerves As a matter of fact this lack probably also holds for the larger vessels Enlargement of the lumen of these vessels is accomplished by vasodilator neurons within the sympathetic division by inhibition of sympathetic constrictors or by chemical substances with a dilatory effect

Peripheral Parasympathetic Vasodilator Nerves to the Skeletal Musculature More recently Kure[152–154] redirected attention to the existence of a so-called fourth group of parasympathetic efferent fibers with a vasodilator action on the vessels of the skeletal muscles (p 134) Earlier publications by Stricker[157–159] Grutzner and Haidenhain[4] Morat[154] Hasterlik and Biedl[7] Werziloff,[165] Ranson and Wightman[168] Bayliss[3] and Hartman Blatz and Kilborn[6] dealt with these fibers

enlargement of the right heart developed only in the final period of his life, about 4 years He succumbed to the combined effects of unrelieved pulmonary hypertension and progressive loss of ventilating surface The autopsy disclosed an extensive and diffuse fibrosis of the pulmonary capillary alveolar bed [150]

Similar cases are met with in the diffuse, what might be termed the centrifugal, type of fibrosis, for example, in certain forms of silicosis or in diffuse parenchymatous fibrosis from any other cause In all these instances, pulmonary hypertension is an accompanying feature but the dynamics of the general circulation may escape alteration for a long time

Quite in contrast is the state of affairs in conditions of direct obstruction of the pulmonary circulation, as in chronic mitral disease Here the parenchyma of the lungs suffers little or very late, whereas the pulmonary circuit is the site of marked hypertension [150] The clinical features of pulmonary hypertension are not always present Thus two groups are observed (1) long standing mitral disease showing little if any clinical evidence of pulmonary hypertension, and (2) chronic mitral disease with marked manifestations of hypertension in the pulmonary circuit

H S aged 32 had been admitted six times to Montefiore Hospital in the period from 1929 to 1942 for recurrent attacks of congestive heart failure It was known that he had had rheumatic heart disease for at least fifteen years and for thirteen years his heart was greatly enlarged the signs of mitral stenosis and insufficiency were unmistakable He had never had an elevated arterial blood pressure In January 1942 the diagnosis of advanced buttonhole mitral valve disease was again confirmed His heart was much rotated the right ventricle was huge and the left ventricle greatly enlarged auricular fibrillation persisted Yet despite this advanced and long standing mitral obstruction pulmonary hypertension had produced no clinical features such as cyanosis polycythemia clubbing of the fingers or other manifestations pointing to any marked impairment of the capillary alveolar bed

V A a 53 year old female was under observation for advanced rheumatic heart disease at Montefiore Hospital from February 1933 until the time of her death in February 1936 There was an intimation that she had had heart disease as a very young child At the age of 24 a diagnosis of stenotic mitral valvular disease was established and she was started on digitalis Her cardiac condition progressed very slowly however and she remained practically free of signs of heart failure In her middle forties she developed a deep and steadily progressive cyanosis limited to the face ears lips and fingers and toes By this time her heart had become large and showed the contour characteristic of advanced mitral obstruction She began to exhibit other signs of progressive impairment of pulmonary ventilation namely intense polycythemia and dyspnea but congestive failure was still not a feature Marked cardiac insufficiency appeared toward the close of her life in striking contrast to the relatively mild insufficiency of the preceding three decades The autopsy disclosed a greatly enlarged heart with healed and recurrent rheumatic involvement of the mitral and pulmonary valves and in addition marked arteriosclerosis of the pulmonary tree extending into the small arteries and arterioles

In this case of *long standing mitral stenosis pulmonary hypertension* was well borne over many years and with little if any cardiac failure With the advent of extensive involvement of the pulmonary arterioles and capillaries the

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Parasympathetic Cardio Inhibitory Fibers Free of controversy, however, is the function of the parasympathetic cardio inhibitory fibers (Fig 18) Stimulating these nerves exaggerates the inhibitory or slowing action of the heart rate Removing the opposed influence of the sympathetic accelerators markedly retards the heart rate, but this is temporary The administration of atropine or severing the parasympathetic cardio inhibitory fibers releases the unrestricted action of the sympathetic cardio accelerators, and the heart beats faster For details on the finer distribution of sympathetic and parasympathetic fibers to the intrinsic cardiac structures see Otto,[167] Rothberger,[1 1 1] Wiggers [06] and Drury and MacKenzie [50]

Parasympathetic Constrictor Fibers to the Vessels of the Heart Although the nervous regulation of the coronary vessels of the human heart is still a subject of study and even controversy, the general consensus based on experiments in dogs is that these vessels are constricted by vagal fibers (Anrep [3] Rein,[163] Wiggers[208])

The parasympathetic as well as the sympathetic innervations to the coronary vessels have a direct bearing on the blood supply to the normal and abnormal heart The nervous controls of the heart as a whole are concerned with more than the regulation of its blood supply These controls operate also on the mechanics of the heart, e g , changes in frequency, minute volume and arterial pressure and these are factors which influence the load imposed upon the heart and more especially the metabolism of the heart

The basis for judging the adequacy of the coronary circulation is not merely coronary flow in relation to the work of the heart but coronary flow in relation to the oxygen consumption of the heart This has been stressed by Gollwitzer Meier and Kruger [67] [68] Their conclusions, the result of studies of the nervous influence on the metabolism of the dog's heart, may be summarized as follows The coarse adjustment of the coronary supply is accomplished by the aortic pressure, more delicate adaptation of the coronary flow is attained by the autonomic innervations to the coronary vessels Stimulation of the sympathetics and adrenalin injection greatly increase the metabolism of the heart However, both factors augment the coronary flow especially as a result of the elevation of arterial pressure This increased flow is marked enough to offset the danger of any insufficient supply of oxygen to the *normal* myocardium

Stimulation of the vagus and of the carotid and aortic inhibitory reflexes undoubtedly depresses coronary flow but even more markedly the metabolism of the heart, as a consequence, these inhibitory regulations never result in a deprivation of oxygen to the normal heart Two conditions in particular may threaten the essential oxygen supply to the normal heart a marked fall in systemic blood pressure causing an unfavorable disproportion between coronary flow and oxygen consumption, and an acceleration of the heart rate leading to an increased cardiac oxygen consumption without a parallel increase in coronary blood supply

These newly established experimental findings emphasize the important consideration that synergic activities of the sympathetic and parasympathetic innervations to the coronary vessels play their part in safeguarding the oxygen supply to the heart The autonomic nervous controls of the coronary flow should also be taken into account in evaluating the concept that anoxemia of the heart muscle is the cause of anginal pain

Parasympathetic Constrictor Fibers to the Hepatic Veins Mautner,[137-140] Mautner and Pick[143, 144] and Molitor and Pick[135] believe that parasympathetic constrictor fibers supply the hepatic veins It is of interest that the blood vessels of the pancreas are supposed to undergo parasympathetic constriction as in the case of the coronary vessels (For a discussion of the innervation of the splanchnic vascular system see p 121)

C Receptor Apparatus for Intrinsic Circulatory Reflexes

Arterial or Sino-Aortic Receptors A group of specially differentiated receptors (sinuses) in the aortic arch and at the bifurcation of the common carotid artery are considered part of the autonomic nervous system Variations in arterial pressure as well as chemical stimuli evoke reflex adjustments in the circulation at large through these receptors Intrinsic reflexes are also initiated by receptors disseminated in the walls of many other vascular channels—the vena cava the auricles and the pacinian corpuscles of the mesentery The carotid and aortic sinus receptors constitute two main stations for the initiation of intrinsic reflexes Of these stations the aortic situated in the aortic arch is the major (Fig 14)

Aortic sinus From this nerve plexus or sinus a nerve ascends to the vagal trunk ganglia and nerve dendrites enter the medulla In lower forms this nerve branch known as the depressor or aortic nerve and clearly described in the rabbit by Cyon and Ludwig[39] is readily identified Its delineation in man is difficult Some authorities are still in doubt about its origin and whether it is a sympathetic or parasympathetic structure However the present consensus holds the nerve to be vagal

It is no longer doubted that the aortic sinus mechanism initiates depressor (parasympathetic) manifestations * Figure 15 depicts the depressor effect on blood pressure which follows excitation of the so-called aortic or depressor nerve This nerve conveys afferent impulses registered at the aortic receptors With

* That depressor manifestations in general may sometimes have a sympathetic adrenergic origin is suggested by a marked decline in blood pressure seen to follow the cutting of both ... (Pike[*]) The same phenomenon had been noted by von Brücke[*] in certain experimental animals the hypotension was accompanied by a retarded heart rate (see p 110 for other examples) A depressor adrenergic reaction for example dilatation of the denervated pupil induced by the intravenous injection of acetylcholine was demonstrated by Bender[*, *] These phenomena belong with the mechanism of *reciprocal* inhibition (Bayliss[1]) and open up an interesting vein of speculation (p 110)

trigger like readiness, the aortic sinus reflexes can be touched off and alteration in systemic blood pressure, as well as other cardiovascular responses, follow These responses are depressor in nature and therefore cholinergic, but it has been claimed that pressor (adrenergic) reactions are sometimes initiated by the

Fig 14 Sino Aortic Sinuses and Their Connections

aortic receptors (Danielopolu[41]) Because of its sensitivity in registering fluctuations of intra aortic pressure, the aortic arch may be compared to a sensitive tambour Most physiologists agree that the variations in aortic pressure act as the chief provocative stimulus for the aortic sinus reflexes (Verworn,[193] Hering [79] [80] Bayliss [14] Heymans and Ladon [93] Adrian [1] Verzar and Peter,[199] DeBurgh Daly and Verney,[45] [47] Bronk [77]) but Lyster and Hooker[56] were not able to confirm this An 'aortic body" or glomus reactive to chemical stimuli has been identified at the base of the heart (Nonidez[156])

Carotid sinus Lying at the fork of the common carotid artery and giving rise to responses similar to those of the aortic receptors the carotid sinus (Fig 14) also contains receptors sensitive to fluctuations in arterial distention and to chemical stimuli Variations in arterial pressure affect the carotid sinus receptors Receptors sensitive to chemical change are alleged to reside in a separate organ the immediately adjacent carotid body This arrangement does not hold for all species The carotid body has been thoroughly described by Meijling[148]

From this sinus or plexus a carotid nerve travels upward into the glossopharyngeal nerve and together with vagal connections reaches the medulla (Fig 14) The superior cervical sympathetic ganglion sends an efferent nerve fil

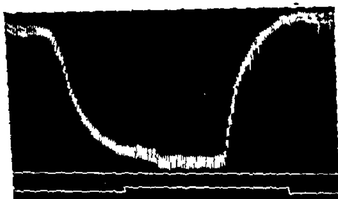


Fig 15 — Typical depressor curve of blood pressure upon excitation of the aortic or depressor nerve The drum was stopped in the middle the curve and the excitation maintained for seventeen minutes The line of zero pressure should be 30 mm lower than shown here Time in 12-second intervals Record to be read from left to right (Bayliss The Vasomotor System London Longmans Green 1923 Reproduced from Macleod Physiology in Modern Medicine 8th ed St Louis Mosby 1938)

ament to the sinus Described by *Hering*[79 80] later by his co-worker Koch[117 119] and by the Belgian group of investigators headed by Heymans[85 86 87] the carotid sinus as a regulator of circulation has been the object of a great deal of study As we shall see in a moment it can give rise to depressor or pressor manifestations

A fall in carotid sinus pressure is followed by vasoconstriction of almost every vascular circuit in the body The vasoconstriction is reputed to have been observed in the following structures in the intestinal vessels Moissejeff[154] Heymans Bouckaert and Dautrebande[87 89] in the head Heymans and Bouckaert[85] in the liver Heymans and Bouckaert[85] in the retinal arteries Collwitzer Meier and Schulte[69] (Michail and Vancea[149] claim that a lowered pressure in the carotid sinuses produces no change in the retinal vessel although a general

fall in blood pressure does alter the retinal vessels), in the femoral veins, Heymans and Bouckaert[83] in the intestinal veins, Fleisch[60, 61] Vasoconstriction has also been reported in the coronary and pulmonary vessels, but this is questionable, since sympathetic stimulation and the consequent rise in blood pressure tend to augment coronary blood flow

The generalized effect of the carotid sinus on circulation also takes a depressor form, most of the vessels of the body undergoing vasodilatation, a fall in venous pressure may be marked Hering[79] elicited this type of vasodilator reaction by stimulating the carotid sinus

Differences in vasoconstriction and vasodilatation occur in different animals and under varied conditions of experimentation and this is also true for the reactions set off by the aortic sinus Both the carotid and aortic sinus reflex mechanisms are not only physiologically analogous but they possess common anatomic features Both sinuses do not arise from the heart but are developed from the primitive branchial arches, in both sinuses the nerve fibrils are alleged to be of a type found nowhere else (de Castro[11, 35]) Tello ([191]) made it clear that the aortic nerves develop at a later state of embryonal life after the aortic arch derived from the sinistral fourth branchial vessels, is well differentiated

Cerebral Circulation At first the cerebral vessels were not considered to be under the pressor influence of the carotid sinus (Heymans and Bouckaert[84]), but this original premise has given place to an opposite opinion established by Bouckaert and Jourdan [5] The circulation of the brain is profoundly affected by the general circulation, and vice versa It is therefore not surprising to find the arteries of the head involved in reactions associated with a drop in general blood pressure (Anrep and Starling[3] Heymans and Bouckaert[8]) Guernsey, Weisman and Scott[75] observed that the effects of increased intracranial pressure *were diminished by the carotid and aortic reflexes* (*For the blood supply to the brain consult* The Circulation of the Brain and Spinal Cord A Symposium on Blood Supply Research Publ A Nerv & Ment Dis Vol 18 1937)

The circulation of the brain is protected by the reflexes of both the carotid and aortic sinuses A striking example of how the aortic sinus may guard the cerebral blood supply is illustrated by the ox, in whom this sinus lies at the origin of the vertebral artery which carries blood to the circle of Willis (de Castro[34] van Damme[197]) The significance of an adequate blood supply to the brain may be witnessed in experimental procedures on nonhuman species Whereas *bilateral ligation of the common carotid arteries in man is fatal* this procedure in the goat merely produces a prompt though temporary loss of consciousness the vertebral arteries in this animal adequately supplying the brain The ancient Greeks were aware of this reaction in the goat Bilateral ligation in the cat hardly disturbs the animal the aortic nerve plexus and vertebral arteries protecting the cerebral circulation

The regulatory influence of the carotid sinus on the brain vessel in general, and surely in man is far from negligible Indeed the carotid sinus may be called the watch dog of the cerebral circulation However it is not the sole guardian In man an important responsibility of this sinus is the compensation by reflex adjustments for the change in the force of gravity which accompanies the erect posture

In many respects if not altogether, the carotid sinus may be said to be complemental to the aortic This is borne out by the simple observation that bilateral denervation of the carotid sinuses still leaves the animal with practically all its vital and extensive cardiovascular regulations

The carotid sinus reflexes are responsible for a variety of activities. These are expressed as changes in the cardio-inhibitory center in the center regulating blood pressure in the center controlling adrenalin discharge in the respiratory center and perhaps in some center or area which may govern the onset of syncope As a rule all or most of these effects will occur at one time but in a number of instances only a few or even a single manifestation may be present

Depressor Manifestations of the Carotid Sinus A sudden elevation of local blood pressure either spontaneous or following compression at the site of the sinus will usher in depressor reactions (Fig 16) The heart rate will very likely be retarded the general blood pressure will fall as a consequence of general vasodilatation the secretion of adrenalin becomes inhibited respirations will be inhibited and sudden syncope may be part of the picture

In comparatively rare instances syncope alone appears after stimulation of the carotid sinus The absence of concomitant cardiovascular reactions in this connection as reported by *Ferris Capps* and *Weiss*[44] suggests that in some cases afferent impulses from the carotid sinus may be able to travel directly to an independent part of the brain concerned with consciousness

Such a possibility raises the thought that syncope may not always be an expression of cardiovascular depressor phenomena and that it is perhaps mediated by a reflex arc well outside the centers associated with cardiovascular regulations By the same token the isolated occurrence of cardiovascular manifestations i e bradycardia or a sudden hypotension following carotid sinus stimulation may perhaps point to the existence of individual groups of afferent neurons connecting the carotid sinus to specific medullary centers for each of these responses

Clinical observations have established that mechanical stimulation of the normal carotid sinus brings on a prompt fall in systemic blood pressure of less than 10 mm Hg This fall is exaggerated if the sinus is hypersensitive Three types of clinical cases have been identified (1) cases of asystole or sudden retardation of the pulse with or without a drop in systemic blood pressure (2) cases of marked fall in systemic blood pressure without marked slowing of the pulse (3) patients with a change in cerebral circulation associated with

fainting and sometimes with convulsions with or without a pronounced effect on the heart rate or blood pressure

The syndrome associated with hypersensitivity of the carotid sinus has been attacked surgically, or by applying a local anesthetic, and often with success Denervation is carried out by resection or by chemical measures In

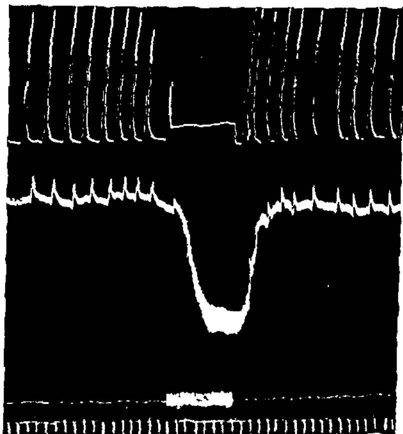


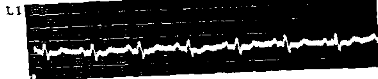
FIG 16 —The effects of external pressure on the left carotid sinus of a dog under chloralose anesthesia Apnea and hypotension resulted (Macleod Physiology in Modern Medicine 8th ed St Louis Mosby 1938 Record made by C F Schmidt and reproduced with his kind permission)

some cases it is necessary to remove the carotid body The following are two cases with fairly characteristic reactions

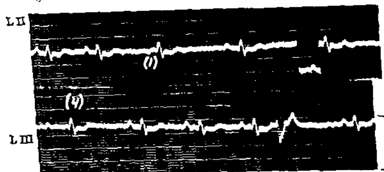
A case of carotid sinus syndrome exhibiting asystole and vertigo M R a male patient at Montefiore Hospital aged 52 had hypertension of at least seven years standing His blood pressure ranged at levels of about 240 systolic and 140 diastolic He also had emphysema and hyperactive reflexes the latter as a residual manifestation of a right hemiplegia suffered in April 1941 In August of the same year he was stricken with a left hemiplegia In recent months he developed marked dizziness when lying flat in bed and turning his head to one side The right carotid sinus became extremely sensitive setting off asystole and dizziness

n on slight pressure but without loss of consciousness This reaction as a rule was ac panied by blanching of the skin of both sides of the face

Lead 2-continuous strip Normal



Right carotid sinus pressure



Left carotid sinus pressure

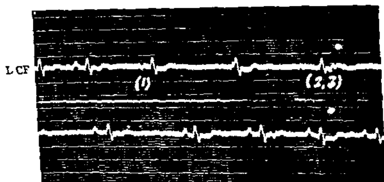


FIG 17 —*Effect* of External Carotid Sinus Pres ure Patient S M Note the 1 placement of the pacemaker from the S A node to the auricle (1) and A V node (3) with depression cf the S-A node (2 3) or sinus block The PR interval (4) is increased

A case f carotid si us synd o e with depressor react on of the bl od pressu e and pulse rate L S a male aged 64 admitted to Montefiore Hospital in 1934 for acute polyarthritis and hypertension was rea lmitted in 1935 for epigastric pain an l for the recent onset of dizzy spells initiated without warning and of brief duration In 1939 the hospital record states

he had an advanced generalized arteriosclerosis polyarthritis and hypertension Readmitted recently it was observed that he experienced numerous episodes of sudden vertigo often in conjunction with anginal seizures but without loss of consciousness Similar attacks were precipitated when the head was quickly turned to one side and also when external pressure was applied to either carotid sinus Pressure over the right carotid sinus for example induced a drop in the blood pressure from 162/88 to 130/66 and a lowing of the pulse rate from 78 to 60 but a rise in the respirations from 20 to 24 excursions per minute

Pressor Manifestations of the Carotid Sinus An abrupt fall in blood pressure at the site of the carotid sinus sets in motion pressor activities This sudden lowering of the local blood pressure is not to be interpreted as causing stimuli *which call forth pressor effects On the contrary, the drop in blood pressure* merely makes it impossible for the sinus to receive an adequate quantity or intensity of stimuli essential for preserving a normal level of systemic blood pressure or an increased local intravascular *pressure* essential for evoking a lowered systemic pressure A lowered blood pressure at the sinus brings about a cessation of depressor stimuli and as a consequence evokes a pressor response The pressor reactions are as follows the heart rate is quickened, the general systemic blood pressure mounts as a consequence of an increase in general peripheral constriction, the output of adrenalin is augmented, respirations are stimulated, and the blood reservoirs, as a result of contraction of the large veins are apt to become emptied In contrast to those called forth by stimulation of the carotid sinus these effects are adrenergic in nature

The primary function of the carotid and aortic sinus reflexes is to help preserve *the fundamental the so called residual or resting vagal tone of the circulation* But it would be more correct to look upon this residual tone as a normal state of function achieved by the activity of reciprocal innervations It is conceivable that in some individuals the carotid sinus reflexes may consist predominantly either of cholinergic or of adrenergic activities This might occur if the specific afferent neurons in question, from the sinus to the medullary centers were increased in absolute number or if the normal number of either group of fibers was reduced The possibility of interplacements or interlacing of adrenergic and cholinergic fibers has already been alluded to but this seems to be a very rare possibility in connection with the carotid sinus With regard to the depressor nerve however anatomic *deviations leading to a preponderance* of vagal or sympathetic neurons is not unknown Danielopolu[44] described combined vagal and sympathetic fibers in the depressor nerve of the dog, he attributed the retardation of the heart to the action of vagal fibers and the change in blood pressure to that of sympathetic fibers

D Venous Intrinsic Reflexes

The venous channels also contain receptors for initiating systemic circulatory changes Examples of this are the Bainbridge reflex[6] and the McDowall reflex[145] They are the equivalent of intrinsic arterial reflexes The Bainbridge reflex

is manifest when a sudden elevation of venous pressure, acting upon the receptors in the auricles and in the large veins causes an acceleration of the heart rate by contrast a depression of venous pressure causes slowing of the heart High venous pressure is said to cause stimulation of the cardiac sympathetics

The McDowall reflex also comprises vasomotor reactions attendant upon variations in venous pressure A fall in venous pressure as after hemorrhage sets in motion a vagopressor reflex and the arterial blood pressure will begin to rise In a later publication McDowall[146] went on to show that this vagopressor reaction is in evidence after severe hemorrhage even when the arterial as well as the venous pressure drops With the return of a mounting level of venous pressure a reflex stimulation of the vasoconstrictor mechanism occurs and arterial tension rises Venous hypertension therefore seems able to induce a reflex vasomotor constriction The pressor pathway for this act probably begins in the right auricle According to Reed and Layman[147] the McDowall reflex will not always come off

A *labyrinth reflex* described by Spiegel[148] represents a specialized reflex Stimulation of the labyrinth by caloric or galvanic stimuli or by rotation induces a fall in blood pressure by a mechanism similar to that evoked on *stimulating* the aortic (depressor) nerve The labyrinth reflex acts on vasomotor *centers* and mainly on the splanchnic vessels The afferent pathway *is by way of* the vestibular nerve (Fig 18) An oculomotor reflex brought *on by* pressure on the eyeball also causes a generalized fall *in* blood pressure

E Peripheral Regulation by Means of Extrinsic Cardiovascular Reflexes

Extrinsic reflexes constitute a group and their activity is mediated without receptors and *without any* known neurons Although possessing no anatomic receptors in the vascular apparatus the extrinsic type of reflex may nevertheless have to be grouped under the functions *of the autonomic* nervous system A variety of reactions *largely chemical* but also physical and mechanical takes place in the tissues *of the body* and *the effects are reflected* in the hemodynamics of the circulation By their lability and their dependence on prerequisite levels of chemical and physical conditions reactions of this type in a very physiologic sense are *rightly designated* as reflexes Whether these reactions however are ever *completely independent* of a direct control by the autonomic nervous system cannot be said

Hormones and other *chemicals act in* the ever changing scene of biologic events going on in the tissues but for all we know they *may* act with or without the *autonomic* nervous system Metabolites in denervated carotid and aortic preparations for instance *can still influence* the reactivity of brain centers i e the *sympathetic vasoconstrictor* and the parasympathetic vasodilator centers Since it is known that *metabolic functions are regulated* in

some manner by the hypothalamus, the suggestion is not out of place that the autonomic nervous system, especially the higher centers including the hypothalamus, may have a hand in governing the chemical reflexes of the circulation

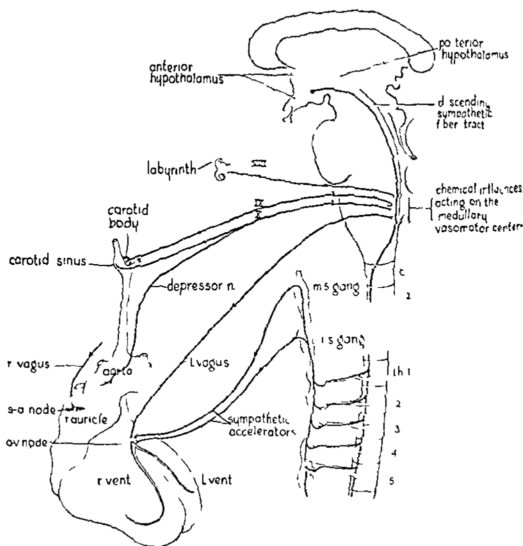


Fig 18 —Schema of the Autonomic Regulations of the Cardio Aortic Apparatus Cortical and hypothalamic elements described in the text (p 105) have not been included in this drawing The basis for the intrinsic cardiac connections as drawn above rests almost wholly on pharmacologic evidence The anterior and posterior hypothalamic regions appear to give rise to general cardiovascular effects

The individual needs of the body must be satisfied by the delivery of appropriate amounts of blood to the various tissues and organs All tissues and every organ obtains its allotment of blood while the blood stream as a whole with its complicated gradients of pressure velocities, etc pursues its course

at an optimal level of efficiency All this is achieved by a large group of extrinsic and intrinsic cardiovascular reflexes and by the closely allied processes of respiration and metabolism

Extrinsic and intrinsic reflexes confer upon the circulation an ability to preserve its normal internal equilibrium but also to meet abnormal conditions within and outside the body For example, the circulatory changes ushered in by hemorrhage shock or the severe loss of fluids, consist of a correlated interaction of both sets of reflexes Again the adaptation of the body to external temperature is largely the result of reflex activities of the circulation The blood pressure and other hemodynamic states are preserved by a coordinated group of fractional i e localized autonomic reactions acting upon the entire circulation

Autonomic Central Controls

Beautifully adjusted and interlocked all the features described above are coordinated into a smoothly moving chain of events In this coordination central stations of the autonomic nervous system play a prominent part Throughout the neuraxis—in the cortex in the spinal cord especially in the bulbar and pontine regions and in the diencephalon—spatial units for cardiac and vasomotor activities are found

A Cortical Bulbar and Spinal Controls

The concept of special centers in the brain for controlling blood vessels first came from Schiff[173, 1 4] The credit of actually discovering such a central area belongs to Ludwig and his pupils especially to Owsjannikow[154] who identified a center in the medulla of the rabbit It was located near the fourth ventricle above the tip of the calamus scriptorius The classic studies of Ludwig and his pupils on rhombencephalic vascular control are almost universally accepted although a few like Muller and Glaser[155] and Scott and Roberts[1?] disagree

An animal with its intact rhombencephalon separated from the mesencephalon will preserve its fundamental cardiovascular responses practically undisturbed Obviously the indispensable central regulation of the cardiovascular apparatus must lie below the mesencephalon Though neither cortex nor even diencephalon are absolutely necessary it must not be concluded these regions are devoid of influence

Cortical Control As early as 1855 Schiff observed the acceleration of the heart rate following stimulation of the frontal lobes and later Danilewsky[45] obtained the same result Bochefontain also found changes in blood pressure and heart rate on stimulation of the cortex he stated that his teacher Vulpian, was aware of this reaction even before he himself published his own result Eulenburg and Landois[54] noted changes in the skin vessels on stimulation of the cortex and changes in blood pressure were reported by Bechterew and

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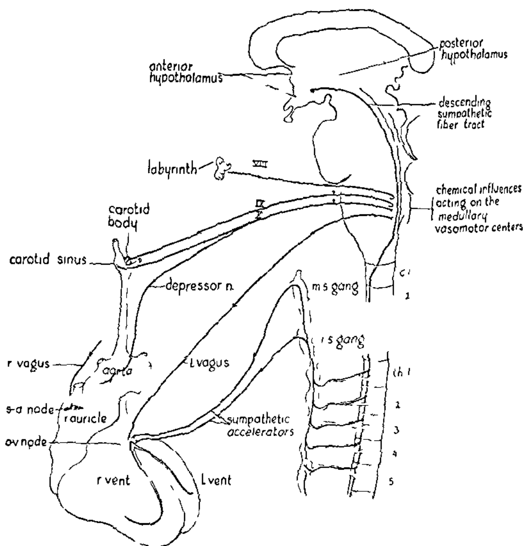


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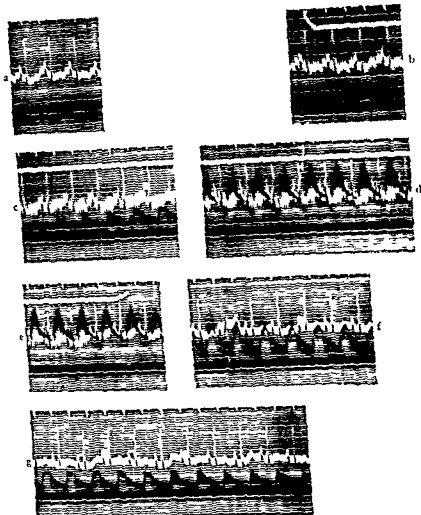


FIG. 19. Hypertension from Cortical Stimulation. Blood pressure and electrocardiographic changes following electrical stimulation of the cerebral cortex of the cat. The cat was kept under light ether anesthesia, artificial respiration was *instituted*, and the animal was then curarized. The dura having been incised and laid wide *open*, the left anterior sigmoid gyrus was stimulated employing a Harvard inductorium with the coil at a distance of *2 cm.* and an input current at 2 volts. The time is *indicated* on the records at intervals of 0.1 second. Lead II was taken throughout.

a. Before stimulation. Blood pressure is 125 *mm.* Hg. T wave negative.

b. Stimulation begun as indicated by the marker. Blood pressure is 125 mm. Hg.

c, d, e. Taken during continuous stimulation of 8.3 seconds duration. Blood pressure *rose* ec c141 t 250 mm. Hg. T wave is negative at the termination of the stimulation (record e).

f. Three seconds after stimulation was stopped. Blood pressure is 100 mm. Hg. T wave *upright*.

g. Six seconds after stimulation was stopped. Blood pressure is 160 mm. Hg. T wave *upright*.

(From a study carried out by Spiegel, Miller, Krueger and Alper.)

Mislawsky,[21] and by François Franck [6, 63] Dusser de Barenne and Kleinknecht[51] observed a rise or fall in blood pressure on stimulating different areas in the region of the sigmoid gyrus Although motor reactions usually accompanied these vasomotor effects, the latter sometimes were elicitable without the former More recently, Fulton[64] obtained changes in arterial pressure on stimulation of the motor and premotor cortical areas Hoff and Green[91] and Green and Hoff [3] described changes in blood pressure from cortical stimulation in curarized and noncurarized animals These observations pointed to cortical effects on blood pressure and on muscular hyperactivity (convulsions) which were independent of each other On stimulating the orbital surface of the frontal lobe in cats and monkeys at an area in the orbital gyrus near the olfactory tract, Bailey and Sweet[5] registered a rise in blood pressure, as well as inhibition of respiration and a decrease in the tone of the gastric musculature

Clinicians long suspected that pathologic changes in the cortex might be acccompanied by derangement of the systemic blood pressure Observations on blood pressure in acute hemiplegias by Kahler[109] and Popper[164] did not *furnish convincing evidence of such a relationship On the other hand,* Bucy [9] noted the absence of blood pressure and radial pulsation on the contralateral side promptly after cortical lesions, the unaffected side remaining normal in this respect Such findings were absent in chronic cases of hemiplegia According to Bucy, the vascular changes on the paralyzed side were due to a generalized constriction of the vessels on this side

The effect of cortical stimulation on arterial blood pressure may be seen in Fig 19

Bulbar Control The bulbar or medullary mechanisms for vasoconstriction and for vasodilatation are usually regarded as a single or common vasomotor center However, the separate identity of each of these physiologic functions *cannot be questioned nor can their intimate and reciprocal interrelationships* The vasoconstrictor apparatus is characterized by a constant tonic discharge, the vasodilator nerves exhibit little or no tonic activity In addition to this vasomotor region, the rhombencephalon contains the cell bodies of the para sympathetic cardio inhibitory fibers Finally, whereas the lower neurons of the sympathetic accelerator cardiac fiber pathway arising in the grey matter of the lateral horns of the higher thoracic segments have long been identified it now appears that the upper neurons of this pathway may consist of fibers which originate in the hypothalamus and descend intraspinally to the thoracic levels (Beattie et al [16, 17])

The association of circulatory derangements with disturbances in the rhom bencephalon and in the brain in general scarcely calls for extended comment Bulbar involvement with its threat to respiratory and cardiovascular functions is a dread complication, very often fatal On the other hand chronic bulbar disorders may *last for years, provided the repositories* in the brain stem which regulate the activities of these vital functions remain intact or nearly so

and Sheehan[19] Ranson et al [166] Kabat et al [107] and Masserman and Haertig[136]) On stimulating the tuber nuclei Beattie[15] obtained a lowered heart rate and a prolongation of the AV conduction time The identification of a circumscribed parasympathetic zone in the anterior hypothalamus, as proposed by Beattie and his collaborators has been controverted by Ranson and his school, and by Crouch and Elliott The latter could never obtain slowing of the heart constriction of the pupils abnormal salivation or other features of cholinergic excitation by stimulating a so-called parasympathetic area

(7) *Evidence of the existence of a parasympathetic zone from intraventricular experiments* A certain body of evidence however tends to support the contention of a parasympathetic zone in the hypothalamus Dikshit[45] claims the hypothalamus exercises a parasympathetic influence on the cardiovascular apparatus Upon injecting acetylcholine into the lateral and third ventricles he provoked a rise or fall of blood pressure depending upon the size of the dose employed Observations of a similar nature were made by Suh Wang and Lim[190] and by Silver and Morton[18] Much earlier Spiegel and Saito[185] had reported a lowered blood pressure from the introduction of pituitrin into the third ventricle of rabbits and Cushing[37] made pioneer observations on the parasympathetic effects in unanesthetized human beings following the intraventricular injection of pituitrin or pilocarpine Although certain cholinergic effects were manifested the blood pressure was not altered in Cushing s experiments but in a later paper[35] he mentions the onset of vasodilatation

While all these results constitute almost positive proof of a central parasympathetic mechanism they do not conclusively prove that the hypothalamus is necessarily a member of the brain stations responsible for this mechanism The introduction of foreign substances into the cerebral ventricles produces general and diffuse effects but precise localization of these (cholinergic) responses is scarcely feasible Moreover even though the cortex and the hypothalamus induce some effect it is possible that the bulk of the cardiovascular responses is mediated through centers no higher than the medulla or the mesencephalon Winkler [0] Waterman[200] van Bogaert[194] Fulton[65] and others showed that stimulation of the cortex causes a rise in blood pressure As is well known the hypothalamus influences blood pressure (Karplus and Kreidl[11] [11] [14]) Spiegel and Yaskin[186] reported that elimination of the diencephalic centers in the cat produced only a transient fall of blood pressure soon compensated and that removal of the cortex alone had no effect on the level of blood pressure After transection caudal to the midbrain the blood pressure increased for four to ten minutes This increase of blood pressure was independent of muscular rigidity and was due to increased reactivity of lower centers to pressor stimuli and to the stimulating effect of the operation

A parasympathetic sphere of influence if we may employ such a designation in a general sense probably does exist in the hypothalamus but its ana

For example a child stricken with a bulbar form of encephalitis or with bulbar involvement due to the effect of diphtheria toxin, or an adult with damage in the rhombencephalon *from hemorrhage or inflammation is likely to survive* if the central regulatory devices are still able to function adequately

Spinal Cord Centers Important subsidiary vasomotor centers or, at least, anatomic areas for the mediation of vasomotor reflexes were identified in the spinal cord by Goltz et al [70–7] Langley,[1 7] Tigerstedt,[19] and Bowen, Coombs and Pike [6] *These will not be dealt with in this text*

B Hypothalamic Control

This control is mediated through adrenergic and chol nergic fiber tracts, by hypothalamo hormonal regulations, by metabolic activities A hypothalamic supervision over the sino aortic reflexes has not been established (For an exposition of the influence of the hypothalamus on circulation and respiration see Hess[81 81 81b])

Sympathetic (Adrenergic) and Parasympathetic (Cholinergic) Manifestations Spatial elements in the hypothalamus responsible for cardiovascular effects are not easy to define accurately A functional differentiation of these elements must exist, since totally different reactions stem from the posterior hypothalamus *as compared, for instance with those from the anterior* hypothalamus or the area just rostral to the latter Beattie [15] has maintained that each district of the hypothalamus—the forward and the caudal—engenders a generalized or mass action, and he has gone so far as to assign to the posterior hypothalamus a sympathetic and to the anterior hypothalamus a parasympathetic character *Neither region, however, is entirely independent, for example the posterior* may be influenced by the rostral (forward) area and inhibitory and augmentory impulses from the cortex and the thalamus probably act on both hypothalamic districts

(1) *Evidence of adrenergic and cholinergic zones in the hypothalamus* *Undoubtedly adrenergic and cholinergic manifestations are called forth by* the hypothalamus under experimental conditions and there is sound reason for believing that the normal hypothalamus participates in the discharge of this dual set of responses Attempts at identifying a specific anatomic locality as the site of origin for each set of reactions encounter difficulties The pioneer investigations of Karplus and Kreidl[111 11] *seemed to suggest a sympathetic* zone or sphere of influence " Later a region of this kind was delineated in the caudal hypothalamus by Bard,[7–9] by Beattie and his co workers [16 17] by Ranson and Wightman [166] and by Crouch and Elliott [36]

From the anterior region of the hypothalamus the following cholinergic manifestations *have been elicited a fall in blood pressure* with the heart seldom slowed (Ranson Kabat and Magoun[165]), contraction of the bladder (Beattie and Kerr[18]) cholinergic effects on the gastrointestinal tract (Beattie

and Sheehan[19] Ranson et al [141] Kabat et al,[70] and Masserman and Haertig[134]) On stimulating the tuber nuclei Beattie[16] obtained a lowered heart rate and a prolongation of the AV conduction time The identification of a circumscribed parasympathetic zone in the anterior hypothalamus, as proposed by Beattie and his collaborators has been controverted by Ranson and his school and by Crouch and Elliott The latter could never obtain slowing of the heart constriction of the pupils abnormal salivation or other features of cholinergic excitation by stimulating a so-called parasympathetic area

(7) *Evidence of the existence of a parasympathetic zone from intraventricular experiments* A certain body of evidence however tends to support the contention of a parasympathetic zone' in the hypothalamus Dikshit[45] claims the hypothalamus exercises a parasympathetic influence on the cardiovascular apparatus Upon injecting acetylcholine into the lateral and third ventricles he provoked a rise or fall of blood pressure depending upon the size of the dose employed Observations of a similar nature were made by Suh Wang and Lim[170] and by Silver and Morton[143] Much earlier Spiegel and Saito[155] had reported a lowered blood pressure from the introduction of pituitrin into the third ventricle of rabbits and Cushing[37] made pioneer observations on the parasympathetic effects in unanesthetized human beings following the intraventricular injection of pituitrin or pilocarpine Although certain cholinergic effects were manifested the blood pressure was not altered in Cushing s experiments but in a later paper[33] he mentions the onset of vasodilatation

While all these results constitute almost positive proof of a central parasympathetic mechanism they do not conclusively prove that the hypothalamus is necessarily a member of the brain stations responsible for this mechanism The introduction of foreign substances into the cerebral ventricles produces general and diffuse effects but precise localization of these (cholinergic) responses is scarcely feasible Moreover even though the cortex and the hypothalamus induce some effect it is possible that the bulk of the cardiovascular respon es is mediated through centers no higher than the medulla or the mesencephalon Winkler [97] Waterman [95] van Bogaert [196] Fulton [55] and others showed that stimulation of the cortex causes a rise in blood pressure As is well known the hypothalamus influences blood pressure (Karplus and Kreidl[112 113 114]) Spiegel and Yaskin[156] reported that elimination of the diencephalic centers in the cat produced only a transient fall of blood pres ure soon compensated and that removal of the cortex alone had no effect on the level of blood pressure After transection caudal to the midbrain the blood pressure increased for four to ten minutes This increase of blood pressure was independent of muscular rigidity and was due to increased reactivity of lower centers to pressor stimuli and to the stimulating effect of the operation

A parasympathetic sphere of influence if we may employ such a designation in a general sense probably does exist in the hypothalamus but its ana

For example, a child stricken with a bulbar form of encephalitis or with bulbar involvement due to the effect of diphtheria toxin, or an adult with damage in the rhombencephalon from hemorrhage or inflammation is likely to survive if the central regulatory devices are still able to function adequately

Spinal Cord Centers Important subsidiary vasomotor centers or, at least, anatomic areas for the mediation of vasomotor reflexes were identified in the spinal cord by Goltz et al ,[70–] Langley,[1 7] Tigerstedt,[19] and Bowen, Coombs and Pike [6] These will not be dealt with in this text

B. Hypothalamic Control

This control is mediated through adrenergic and cholinergic fiber tracts, by hypothalamo hormonal regulations, by metabolic activities A hypothalamic supervision over the sino aortic reflexes has not been established (For an exposition of the influence of the hypothalamus on circulation and respiration see Hess[91 81a 81])

Sympathetic (Adrenergic) and Parasympathetic (Cholinergic) Manifestations Spatial elements in the hypothalamus responsible for cardiovascular effects are not easy to define accurately A functional differentiation of these elements must exist, since totally different reactions stem from the posterior hypothalamus as compared for instance, with those from the anterior hypothalamus or the area just rostral to the latter Beattie [15] has maintained that each district of the hypothalamus—the forward and the caudal—engenders a generalized or mass action, and he has gone so far as to assign to the posterior hypothalamus a sympathetic and to the anterior hypothalamus a parasympathetic character Neither region, however, is entirely independent for example, the posterior may be influenced by the rostral (forward) area and inhibitory and augmentory impulses from the cortex and the thalamus probably act on both hypothalamic districts

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C Hypothalamo Hormonal Control

Enough has already been stated to indicate that the hypothalamus alone hormonal elements in the posterior and anterior pituitary lobes or the inter action of all these factors (a hypothalamo-hormonal interaction) help govern the regulation of water exchange and metabolic processes How far does such a neurohormonal (hypothalamo-hormonal) interaction affect the circulation?

It is quite possible that the hypothalamus may be able to act on the circu lation by sending impulses to the endocrine organs directly, without the inter vention of endocrine elements in the anterior pituitary lobe for example to the thyroid the adrenals the posterior pituitary lobe the gonads We shall not enter into an exposition of these possibilities but any consideration of a hypothalamo-endocrine regulation of the circulation we feel should not gloss over a neurohormonal influence as exemplified by the action of adrenalin, pituitrin may possibly have a similar relationship

Adrenalin This product constricts nearly all the blood vessels of the body (An exception is the vasodilator effect on the coronaries) In very great dilution adrenalin will lead to vasodilatation of vessels usually constricted by greater concentrations of the drug During the sympathetic upheaval which follows the freeing of the posterior hypothalamic region from the influence of the cortex and other parts of the diencephalon adrenalin output seems to be suddenly and inordinately augmented and the blood pressure level is raised This sharp hypertension is in striking contrast to the undisturbed level in the oblongata animal Just how the hypothalamus functions to increase the adrenalin output and elevate blood pressure is not understood Several theoretic possi bilities suggest themselves

First the hypothalamus directly stimulates the secretion of adrenalin from the medulla of the adrenal glands or excites the elaboration of the allied prod uct sympathin at adrenergic nerve endings (In the former instance the hypo thalamus would send impulses through preganglionic efferent neurons and the impulses could go no further than the adrenal glands in the second instance the impulses would be mediated through preganglionic and postganglionic neurons) A second possibility it might be argued entails a change in adrenalin secretion due to sino-aortic reflexes acting through their related medullary centers and perhaps also through some as yet undiscovered hypothalamic centers Lastly although no proof can be marshalled to support this point of view the hypothalamus may activate an adrenotropic element in the anterior pituitary lobe in this way augmenting the discharge of adrenalin However the presence of an adrenotropic hormone in this lobe has not been conclusively demonstrated (Reiss[169])

Experimental Evidence of a Hypothalamo Adrenalin Relationship Bard[7] showed that the posterior hypothalamus presides over a complicated mechanism which removed from the influences of other parts of the hypothalamus and

tomic delineation is still obscure It may prove to be that cholinergic manifestations arise in the hypothalamus not in any particular area but rather as a diffuse and generalized response by the hypothalamus as a whole

Hypertension accompanied by an increase in heart rate has been reported by van Bogaert[193-195], and by Jaegher and van Bogaert[101, 105] after cutting the vagus This type of elevated blood pressure was abolished by severing the sympathetics or by administering ergotamine Disagreeing with Ranson et al [16] Jaegher and van Bogaert insisted that the hypothalamus contains a depressor, *not a pressor area, and that sectioning the vagus or blocking it with atropine* merely removes the activity of the depressor zone, thus inducing a pressor effect passively According to them, this depressor area lies in the caudal portion of the lateral hypothalamic area, and they would not subscribe to any hypothesis that so called 'centers" for cardiovascular regulations exist as distinct zones or areas in the hypothalamus

The Ranson school is in sharp disagreement with this point of view Rioch and Brenner[170] reported that stimulation of the posterior hypothalamus of *decorticated cats give similar results to those described by Ranson* and his co workers, no parasympathetic zone (depressor area) was made out

The cholinergic discharge displays, as a rule, 'fragmentary' reactions (Cannon[31]) This may take the form of accentuating a single function e g, a *fall* in systemic blood pressure, or several functions may be involved

'Overlapping' of Adrenergic and Cholinergic Effects An intriguing point in connection with a dual or divisional physiologic reaction of the hypothalamus revolves about the query Are generalized cholinergic manifestations always depressor in nature, and are adrenergic reactions always pressor? This might seem a far fetched, even futile question, were it not for pressor manifestations occasionally taking the form of a cholinergic response, and depressor manifestations *taking the form of an adrenergic response* Cutting the vagi in some animals (von Brucke [3]) has been known to cause a fall in blood pressure along with a slowing of the heart Pike[161] has made similar observations McDowall[145] found a vagopressor reflex came into operation when *there was a marked drop* in the venous pressure In these examples, a depressor manifestation seems to be associated with adrenergic activity Another example of a vagal (depressor) reaction seemingly adrenergic in nature is the slowing of the heart in man at the height of adrenergic reaction (Hume[99]) These paradoxic and unexpected results are perhaps due to nerve fibers of one chemical system being interlaced with neurons of the opposite division or the results may be explained as examples of the mechanism of reciprocal innervation (see footnote p 95) On the other hand, it is possible, though no proof exists that a common territory, perhaps the hypothalamus, is in a position to cause pressor responses by cholinergic activity as well as depressor reactions as an accompaniment of adrenergic activity

activity are demonstrated without much difficulty. Pituitrin will slow the heart in man (Kountz[120]); it raises the mean blood pressure (Koll and Ceiling[119]); it constricts the coronary vessels (Anrep and Stacey and Goldenberg and Rothberger[66]). These last found the effect very marked in the rabbit. Holtz[87] obtained an increased coronary flow in the cat from pituitrin, and it produces splanchnic constriction accompanied by a reduction of volume of the liver. The diminution of the size of the liver is associated with a dilatation in the hepatic veins in the dog (Mautner and Pick[143]; Lampe and Mehes[125, 126] and Holtz).

Whereas the secretion of the antidiuretic principle of the posterior pituitary lobe depends upon the undisturbed continuity of a bundle of axons running between the hypothalamus and the posterior pituitary lobe, no analogous tract of axons has been identified with respect to the secretion of the pituitary pressor substance. Yet it is tempting to speculate about a pituitary *pressor* ingredient which may function under hypothalamic supervision to regulate the large capillary bed and other cardiovascular structures. This would be analogous to the effect achieved by adrenalin on the arterioles and large vessels through the intervention of the hypothalamus. Experimental data appear to substantiate this hypothesis to some degree. Thus Schurmeyer[191] witnessed melanophore expansion in frogs with hypothalamic puncture and he attributed this to a release of pituitrin. Karplus and Peczenik[115, 116] stimulated the hypothalamus and obtained the release of a substance alleged to be pituitrin in the cerebrospinal fluid, capable of producing contraction of uterine stripes and expansion of melanophores of frog skin.

These observations, however, do not add up to convincing corroboration of a hypothalamo-hormonal control of the pressor ingredient of pituitrin.

Acetylcholine. A brief comment on acetylcholine and on histamine may not be out of place at this juncture. Acetylcholine, in some respects the chemical counterpart of the transmittor product adrenalin, and very likely histamine as well, are associated with autonomic functions. This association, however, cannot be clearly defined with regard to the function of the hypothalamus. The controversy whether this portion of the brain is endowed with a circumscribed parasympathetic zone does *not* weaken the experimental evidence that some cholinergic manifestations arise in the anterior hypothalamus. These responses and whatever ability the hypothalamus as a whole may possess to produce cholinergic reactions are probably bound up with the liberation of acetylcholine at the nerve endings and affector organs and with the transportation of this chemical by the circulating blood stream.

Bender[?, 22] demonstrated an acetylcholine discharge in the frightened monkey. Fright and other explosive emotional states, sham rage for instance, have been linked to hypothalamic hyperactivity. Thus the hypothalamus may after all turn out to be a central instigator of diffuse acetylcholine effects

from the cortex, precipitates a generalized and violent upheaval, a sympathico adrenal reaction In his attempts at isolating the posterior hypothalamus from the rest of the diencephalon and from the cortex, Bard[7] inadvertently left a ventral and posterior segment of the thalamus in situ but attached no great functional significance to this small residual fragment [9] A constant accompaniment of this upheaval or outburst was the occurrence of manifestations suggestive of a sudden increase of adrenalin discharge, 'sham rage"

Upon stimulating the infundibular portion of the third ventricle Houssay and Molinelli[93] obtained a rise in adrenalin secretion Electrical stimulation of the fiber pathways passing from hypothalamic nuclei through the lateral hypothalamic area also provoked a marked elevation in blood pressure as well as an increase in heart rate (Kabat,[106] Ranson, Kabat and Magoun [165] van Bogaert[196]) and although it could not be gainsaid that the adrenal glands were an important factor, the responses were elicited even in the absence of these glands (Fig 22) Confirming the observations of the South American workers Magoun Ranson and Hetherington[131] obtained evidence of an augmented discharge of adrenalin and a release of sympathin* into the circulation when the hypothalamus was stimulated The site of stimulation was the lateral hypothalamic area which consists of fibers of the medial forebrain bundle and except in the caudal part contains comparatively few cells

On the basis of all this it seems safe to accept the hypothalamus as a station capable of exercising a control over the adrenal medullary substance The stimulated secretion of adrenalin, as a rule, is registered by a rise in blood pressure and by an increase in oxygen consumption and an elevation of blood sugar (Beattie[15]) Sudden hypertension an abnormal increase in adrenalin, and hypothalamic activity are therefore probably related

It has been claimed the hypothalamus is also capable of sending impulses directly to blood vessels constricting or dilating them Penfield and Stavraky[160] believed they saw constriction of pial vessels in the meninges of cats when the posterior hypothalamus was stimulated The vessels appeared to be dilated on stimulation of the ventral area of the tuber cinereum

Evidence of a Hypothalamo Pituitrin Relationship An analogy may be made between a neurohormonal effect on the action of adrenalin and that on the action of pituitrin in connection with water regulation The antidiuretic principle of the posterior lobe is certainly under hypothalamic supervision But what evidence is there that the pressor principle of the posterior lobe with its potent constrictor effect on the vast capillary beds of the body is controlled by the hypothalamus?

The question is more readily asked than answered A pressor substance from the posterior pituitary lobe is easily identified and the sites of its cardiovascular

* See Cannon and Lissak[32] for the interesting data on the extraction of adrenalin from neurons of the adrenergic system

D Metabolic Activities and the Hypothalamus

The effects of metabolic activity, reflected in the circulation are quite definite Since the functions of the hypothalamus are not divorced from this activity we must recognize that a certain command over the circulation is achieved by the combined activities of the hypothalamus and metabolism Extensive consideration of the interrelationships between metabolism circulation and respiration is not within the scope of this volume

F The Hypothalamus and Blood Pressure

The hypothalamus as well as other subcortical areas and the cortex cooperate with the peripheral autonomic system in bestowing upon the blood

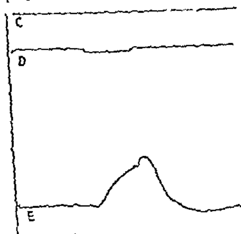


Fig 20 – Abrupt elevation of blood pressure upon stimulation of lateral hypothalamic area *E* is the blood *pressure tracing* (*Ranson* Kabat and Magoun Arch *Neurol* & Psychiat 1933 33 468)

vessel of the body a *constant tonicity* expressed as a stabilized range of systemic blood *pressure* Accordingly *we must look* to the hypothalamus as a participant and perhaps in *some* cases even as an instigator of derangements in blood pressure The *hypothalamic region* however is not to be considered as eclipsing in importance the cardiovascular regulations of the medulla As a sympathetic (adrenergic) *station* the hypothalamus exercises functions which seem to overshadow its parasympathetic (*cholinergic*) activities Many cardiovascular activities are influenced by the hypothalamus but of these chiefly three—blood pressure cardiac rate and cardiac rhythm—will be dealt with below Other activities such as the filling and emptying of blood depots, and perhaps the osmotic pressure may be under autonomic control but no definite role can be assigned to the hypothalamu

at least in the monkey Interesting in this connection are Bender's findings that acetylcholine is not so rapidly neutralized or destroyed in the tissues as has been generally believed

Acetylcholine brings about widely distributed cardiovascular effects The level and range of these effects are in proportion to the size of the dose and depend also upon the type of animal employed In general, extensive dilatation of the blood vessels is the rule, except in the lungs, where it is absent and in the kidneys where it is slight (Hunt[100, 101]) Von Euler[55] produced a rise in pulmonary pressure in perfusion experiments with acetylcholine in dogs, and McDowall[147] obtained a similar result in the intact cat The rise in pulmonary pressure has been ascribed to constriction of the pulmonary veins The spleen, too is supposed to exhibit a constrictor effect from acetylcholine (Farber[57]), and as we have already stated the introduction of this substance into the cerebral ventricles is attended by remarkable generalized cholinergic reactions

Histamine This chemical is considered an agent capable of modifying the peripheral circulation It has the property of causing a remarkable fall in general blood pressure When injected into an anesthetized animal a very extensive generalized dilatation takes place Exceptions to this are the pulmonary vessels and according to Mautner and Pick,[141–144] the hepatic veins These latter vessels are said to become constricted in carnivora, but not in herbivora As the liver veins undergo constriction according to these investigators it may be assumed the splanchnic vessels concomitantly dilate An increased permeability of the capillaries and of the smaller arterioles is supposed to account for the generalized dilatation (Dale and Richards,[4] Bauer and Richards,[11] Burn and Dale[30]) The effects were observed in the dog not in the cat

Of special interest and perhaps pointing to a link between the hypothalamus and the action of histamine are the uncontroverted data connecting the action of this drug with the autonomic nervous system Hogben Schlapp and MacDonald[86] showed that histamine dilates the denervated pupil and Burn and Dale[30] Lewin and Schilf[137] Feldberg,[58] and Mackay[137] demonstrated that histamine is responsible for an initial fall of blood pressure followed by a distinct rise The latter effect has been interpreted as being due to a stimulated increase in adrenalin secretion This sequence of events suggests that a continuing fall in blood pressure, after histamine is offset by an exaggerated compensatory output of adrenalin The adrenal glands, therefore may act to protect the animal against an excessive or protracted hypotension However it has been alleged that the adrenal cortex is more important than the medulla in affording this protection On the other hand there are physiologists who believe all these effects are specific for histamine Practically all the reactions of the cardiovascular system attributed to histamine may be produced with potassium (Pike[16, 163])

and 22) The greatest concentration of points yielding vasopressor reactions on hypothalamic stimulation was located in the lateral hypothalamic area in a plane directly in front of the mammillary bodies (Kabat et al[109])

In addition to vasoconstriction Karplus and Kreidl observed cholinergic reactions i e bladder contraction and lacrimation A dissenting point of view was offered by Hoff and Urban[95] who stated persistent hypertension came from destruction, not excitation of the mammillary bodies

Hypotension Stimulation of the anterior hypothalamus the preoptic area and the septal region leads to a depression of blood pressure although the heart rate is not always slowed (Fig 23) (Ranson Kabat and Magoun[185] and

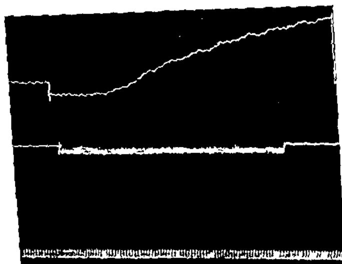


Fig 22 —Rise in blood pressure of an adrenalectomized cat upon stimulation of the hypothalamus (Karplus and Kreidl, Pfluger Arch 1927 *215* 668)

Kabat Magoun and Ranson[108]) According to these workers the hypothalamic region for vasodilatation is influenced by the frontal lobe through corticoseptal fibers described by Wallenberg [200 201] Despite this localization of a depressor effect close to the anterior portion of the hypothalamus the Ranson investigators and Crouch and Elliott[36] were not able to verify the existence of parasympathetic centers in the hypothalamus

In their recent survey of experimental investigations of stimulation of the hypothalamus Ranson Kabat and Magoun summarized the results of painstaking and systematic exploration of the hypothalamus carried out by Ranson and his associates Electrodes were used fo stimulation so constructed as to reduce to a minimum the spread of the effect of the current More than 7 000 points in 50 cats were explored and the reactive points carefully plotted

Hypertension Clinical observers conceived of some form of hypothalamic supervision of blood pressure Schrottenbach[179, 180] was probably the first, Leschke,[1 8] and Castex[33] stressed the same point but substantial proof for such a concept came only with actual exploration of the hypothalamus The discovery that stimulation of the hypothalamus is accompanied by an increased adrenalin secretion fitted in well with the clinical assumption of a hypothalamic regulation of blood pressure Bechterew [0] knew of the relation of higher centers to blood pressure Aschner[4] had noted an elevated blood pressure when the

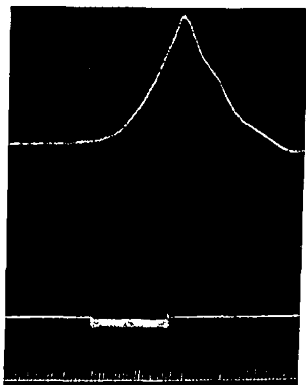


FIG 21 —Rise in blood pressure of a hypophysectomized cat upon stimulation of the hypothalamus (*Karplus and Kreidl Pfluger s Arch 1927 215 668*)

hypothalamus was stimulated Others who laid the groundwork for the belief that sudden hypertension is an expression of excitation of the hypothalamus were Dresel [49] who claimed the mean blood pressure was controlled by hypothalamic centers, Houssay and Molinelli,[98] Karplus and Kreidl,[114] Wang and Richter, [00] Beattie, Brow and Long,[16 17] Kabat Magoun and Ranson [108] Magoun, Ranson and Hetherington[134] and others associated with the Ranson group This type of hypertension was always transient and was held to originate in the caudal portion of the hypothalamus and, according to Karplus and Kreidl was independent of the function of the pituitary and adrenal glands (Figs 21

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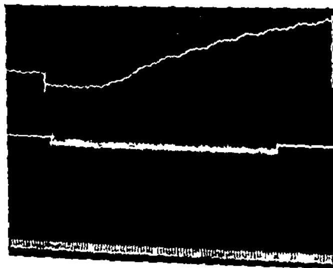


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Many pressor points yielding a marked rise in blood pressure were elicited from the most rostral portion of the supraoptic portion of the hypothalamus, and depressor points in blood pressure were obtained from the preoptic area situated a little more dorsally in the same vicinity Among the latter there were interspersed a number of pressor spots capable of setting off a moderate rise in blood pressure

More caudally, about 2 1 mm back of the zone just described and in a plane passing immediately behind the caudal border of the optic chiasm, a large number of pressor points were identified These points were widespread through the hypothalamus and especially in the lateral hypothalamic area, in the sub fornical element of the medial forebrain bundle, in an area corresponding to

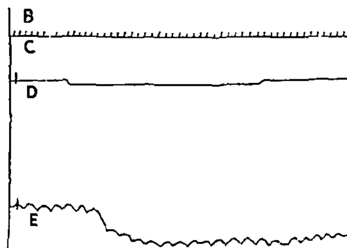


Fig 23 —Fall in blood pressure following stimulation of the anterior region of the hypothalamus *E* is the blood pressure record (Ranson Kabat and Magoun Arch Neurol & Psychiat 1935 *33* 471)

the supraoptic commissures and along a line adjacent to the wall of the ventricle The area of the paraventricular nucleus and the dorsomedial hypothalamic area contained no reactive points, except for a few at the border of the latter area The aggregation of reactive pressor points suddenly grew much larger at the level of the posterior border of the optic chiasm at the level of the supraoptic decussations the reactive zone touched the mid line

Continuing still more caudally for about 4 3 mm in the fresh brain that is covering a distance between the level of the supraoptic decussation and the level of the supramammillary decussation, many points were found in the lateral part of the hypothalamus which upon stimulation induced a marked and abrupt hypertension The medially placed nuclei—the ventromedial and the ventrolateral—contained only very few reactive points The same paucity obtained for the rostral part of the posterior hypothalamic nucleus but at the

level of the tuber cinereum not quite 3 mm behind the level of the supraoptic commissure reactive points were considerably more numerous

Just caudal to this last level the zone of reactive points gradually extended dorsally and medially and invaded the Torel fields and the posterior hypothalamic nucleus as it lies caudal and medial to the Vicq d Azyr tract At the level of the supramammillary decussation many pressor points lay near the mid line The medial mammillary nucleus contained no pressor points at this level (Ranson et al[165])

F Hypothalamic Influence on Cardiac Rate

The rate of the heart is not maintained solely by the cardio-accelerator and cardio-inhibitory fibers The sino-aortic reflexes the level of venous pressure operating through the Bainbridge reflex and the metabolic states of the body are factors The abnormalities in cardiac rate from disturbances set up in the vagal branches to the heart or in the sympathetic accelerator branches are too well known to require extended comment The slow heart of an animal deficient in thyroid hormone or the rapid heart of a hyperthyroid individual is due to a series of metabolic events some of which may be under hypothalamic regulation But in either case retardation or acceleration of the heart rate is accomplished by the transmission of adrenergic or cholinergic impulses to the cardiac pacemaker mechanism and as a rule through sympathetic and vagal cardiac nerves Derangements of heart rate are readily produced by stimulating blocking or severing the vagi these nerves are largely if not entirely under medullary control Similar procedures on the cardio-accelerator fibers also lead to abnormalities in cardiac rate These fibers emerge from the upper thoracic segments of the cord higher neurons those travelling intraspinally from the brain stem to the intraspinal centers are probably represented by the tract described by Beattie Brow and Long

As far as we can tell the variations in heart rate mediated by adrenergic and cholinergic impulses need involve no centers higher than the medulla But we should not lose sight of the fact that variations in rate i e an increase in rate may occur with sham rage and upon stimulation of the posterior hypothalamus[183]

Hypothalamic impulses therefore may be transmitted to the cardiac pacemaker through the blood stream by means of autonomic chemicals—adrenalin (sympathin) and acetylcholine—or the impulses may be conveyed by hypothalamic fiber connections as yet undiscovered to established adrenergic or cholinergic neurons i e the cardio-accelerator and cardio-inhibitory fibers and so to the pacemaker Beattie s observation that stimulation of the tuber nuclei induces slowing of the heart rate and prolongation of the AV conduction time may be interpreted as probable evidence of some type of connection between the hypothalamus and the cardiac pacemaker An effect on heart rate

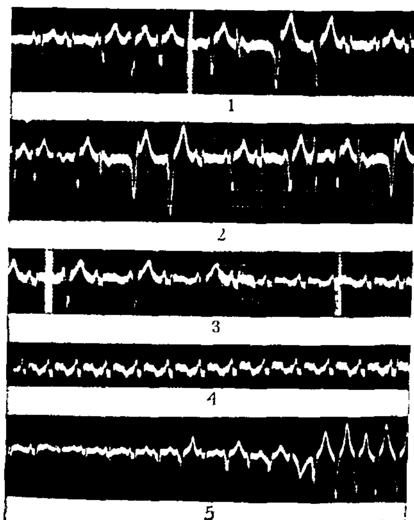


FIG 24 —Electrocardiographic tracings (Lead II) of a cat

1 Cat under chloroform anesthesia showing ventricular extrasystoles auricular rate 240 per minute

2 After section of the anterior part of the hypothalamus Arrhythmia remains unchanged

3 After section of the hypothalamus in the plane joining the anterior edge of the colliculi to the posterior edge of the pituitary fossa Extrasystoles are fading out and normal *rhythm* is appearing auricular rate 180 per minute

4 One hour after the effective section showing persistence of regular rhythm

5 *Extrasystoles produced by stimulation of the hypothalamus*

(Beattie Brow and Long Proc Roy Soc Series B 1930 *106* 253)

following extensive experimental lesions in the hypothalamus was noted by Watts and Fulton [94], and slowing of the heart rate upon stimulation of the anterior hypothalamus was reported by Ranson and his co workers [165]

Fluctuations in cardiac rate are frequently due to blood pressure changes induced by peripheral or central causes Since the hypothalamus is supposed

to affect peripheral constriction (Leschke[1,5] Penfield and Stavraky[169]) and to modify the output of adrenalin it may well be that a hypothalamic effect on heart rate is a consequence of hypothalamic influence on blood pressure Changes in heart rate (sinus bradycardia or tachycardia) are associated with respiratory center disturbances (Heymans et al[88-90]) The heart rate also varies with the state of venous pressure

G Hypothalamic Influence on Cardiac Rhythm

The rhythm of the heart may be altered by a number of mechanisms Of these we shall touch only upon those in which the hypothalamus is possibly implicated

Until recently it was not suspected that the hypothalamus might have a part in preserving the normal rhythm of the heart or in initiating deviations of this rhythm With the discovery by Beattie et al[16-19] of sympathetic efferent fibers which connect the cardiac plexuses to the posterior hypothalamus, a way was opened by which the hypothalamic supervision of rhythm of the heart could be studied In addition to these fibers we shall also discuss, although somewhat briefly the cardio accelerator and cardio-inhibitory fibers the carotid and aortic reflexes the respiratory center and metabolic factors any or all of which may come under some type of hypothalamic supervision as far as the cardiac rhythm is concerned

By means of adrenergic neurons from the posterior hypothalamus Levy[1,5-111] demonstrated that chloroform anesthesia produced extrasystolic activity of the heart and Beattie et al proved that this type of cardiac arrhythmia was readily abolished by placing destructive lesions in the posterior hypothalamus or by interrupting the sympathetic (adrenergic) tracts which emerge from this region Damage or extirpation of the anterior hypothalamic area did not prevent or abolish extrasystolic arrhythmia By demonstrating that electrical stimulation of the caudal portion of the hypothalamus brought on extrasystoles accompanied by a rise in blood pressure the theory of an increased liberation of adrenalin as the cause of extrasystoles received corroboration at their hands Inasmuch as similar results could be evoked in adrenalectomized animals the deduction was made that stimulation of the hypothalamus directly enhances the liberation of an adrenergic sub tance

By means of the carotid and aortic reflexes These reflexes are associated with cardiac irregularities Intact the sino-aortic neurons exert a tonic inhibitory action on the heart under resting conditions Since a blocking or severance of these nerves is answered by a decided rise in heart rate we may be permitted to assume that afferent impulses from the siro-aortic plexuses incite the cardio-inhibitory center (in the floor of the fourth ventricle) and so slow the heart reflexly

Blocking or interrupting the afferent pathways of these reflexes sometimes

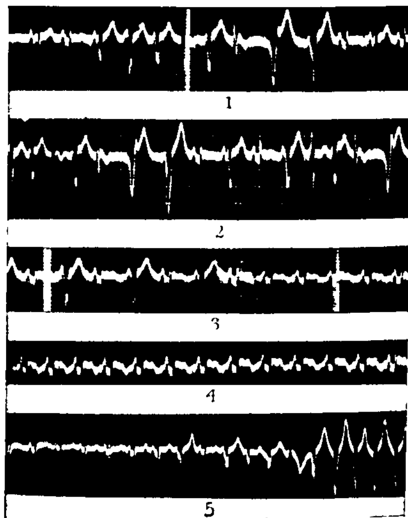


FIG 24 —Electrocardiographic tracings (Lead II) of a cat

1 Cat under chloroform anesthesia showing ventricular extrasystoles auricular rate 240 per minute

2 After section of the anterior part of the hypothalamus Arrhythmia remains unchanged

3 After section of the hypothalamus in the plane joining the anterior edge of the colliculi to the posterior edge of the pituitary fossa Extrasystoles are fading out and normal rhythm is appearing auricular rate 180 per minute

4 One hour after the effective section showing persistence of regular rhythm

5 Extrasystoles produced by stimulation of the hypothalamus

(Beattie Brow and Long Proc Roy Soc Series B 1930 *106* 253)

following extensive experimental lesions in the hypothalamus was noted by Watts and Fulton [94], and slowing of the heart rate upon stimulation of the anterior hypothalamus was reported by Ranson and his co workers [165]

Fluctuations in cardiac rate are frequently due to blood pressure changes induced by peripheral or central causes Since the hypothalamus is supposed

[9] BARD P On emotional expression after decortication with some remarks on certain theoretical views Psychol Rev 1934 *41* 309

[10] BAUER W DALE H H POULSSON L T AND RICHARDS D W The control of circulation through the liver J Physiol 1932 *74* 343

[1] BAUER W AND RICHARDS D W A vaso-dilator action of acetates J Physiol 1928 *66* 3 1

BAYLISS W M On the origin from the spinal cord of the vasodilator fibers of the hind limb and on the nature of these fibers J Physiol 1900-01 *26* 173

[13] BAYLISS W M Further researches on antidromic nerve impulses J Physiol 1907 *25* 276

[14] BAYLISS W M The excitation of vaso-dilator nerve fibers in depressor reflexes J Physiol 1908 *37* 264

[15] BEATTIE J The relation of the tuber cinereum to gastric and cardiac function (A preliminary note) Canad M A J 1932 *26* 278

[16] BEATTIE J BROW G R AND LONG C N H For title see Chapter I reference (1) Res Pbl Ass nerv ment Dis 1930 *9* 249

[17] BEATTIE J BROW G R AND LONG C N H For title see Chapter I reference (8) Res Pbl Ass nerv ment Dis 1930 *9* 295

[18] BEATTIE J AND KERR A S The effects of diencephalic stimulation on urinary bladder tonus Brain 1936 *59* 302

[19] BEATTIE J AND SHEEHAN D The effects of hypothalamic stimulation on gastric motility J Physiol 1934 *81* 218

[20] VON BECHTEREW W Die Funktionen der Nervencentra Vol III *Jena Fischer 1911*

[21] VON BECHTEREW W AND VON MISLAWSKY N Ueber den *Einfluss der Grosshirnrinde* auf den Blutdruck und die Herzthätigkeit Neurol Centralbl 1886 *5* 193

[22] BENDER M B Sensitized pupillary dilator and facial *muscles* as *indicators* of sympathetic and parasympathetic substances in blood Proc Soc Exper Biol & Med 1938 *39* 62

[23] BENDER M B Fright and drug contractions in *denervated* facial and ocular muscles of monkeys Am J Physiol 1938 *121* 609

[24] BOCHEFONTAINE L T Etude expérimentale de l influence exercée par la faradisation de l écorce grise du cerveau sur quelques fonctions *de la vie organique* Arch de physiol norm et path 1876 *3* 140

[25] BOUCKAERT J J AND JOURDAN F Effets de l adrénaline et de l excitation du sympathique cervical sur la circulation intracranienne isolée *Compt rend* Soc de biol 1935 *120* 84

[26] BOWEN R J COOMBS H C AND PIKE F H The effect on blood pressure of removal of portions of the spinal cord in the thoracic *region* *Proc* Soc Exper Biol & Med 1922 *19* 181

[27] BRONK D W Afferent impulses in the carotid sinus and aortic nerves Proc Soc Exper Biol & Med 1931 *28* 1014

[28] VON BRUCKE F T Ueber die reziproke reflektorische Erregung der Herznerven bei Reizung des N depressor Ztschr f Biol 1917 *67* 507

[29] BUCY P C Vasomotor changes associated with paralysis of cerebral origin *Arch Neurol* & Psychiat 1935 *33* 30

BURN J H AND DALE H H *The vaso-dilator action of histamine and its physiological significance* J Physiol 1926 *61* 185

CANNON W B The wisdom of the body New York Norton 1932

CANNON W B AND LISSAK R Evidence for adrenaline in adrenergic *neurones* Am J Physiol 1939 *1 5* 76

[34] CASTEX M R La hipertension arterial *Buenos* Aires An Iretta 1929

[35] DE CASTRO F Sur la structure et l innervation du sinus carotidien de l homme et des mammifères Nouveaux faits sur l innervation *et* la fonction du glomus caroticum Etudes

brings on an extrasystolic irregularity, the extrasystoles originating in either or both ventricles, a terminal ventricular fibrillation sometimes occurs Once established, the extrasystolic arrhythmia is quickly abolished by cutting the adrenergic fibers which descend from the posterior hypothalamus, or by sectioning or paralyzing with ergotamine the adrenergic cardiac innervations which leave the spinal cord Abolishing extrasystoles by removing the influence of these adrenergic cardiac fibers implies that a hyperactivity of this innervation may be related to the cardiac irregularity It has therefore been suggested that the afferent inhibitory (vagal) impulses, which are propagated by the sino aortic nerves, contribute to maintaining a normal cardiac rhythm by opposing or in some other way influencing the adrenergic cardiac nerve fibers

The sino aortic reflexes, however, are mediated through the medulla, so that the arrhythmias of the heart associated with these reflexes include the participation of medullary centers connected with the sino aortic nerves No evidence has been adduced thus far of these reflexes passing through the hypothalamus, the arrhythmias of sino aortic origin, therefore, cannot be ascribed to any hypothalamic intervention However, since the posterior hypothalamus has a well defined efferent sympathetic fiber tract which participates in the provocation and prevention of extrasystoles, the question may be left open whether this tract or the hypothalamus itself may not be related to the neurons over which the sino aortic reflexes are transmitted

Through metabolic activities Cardiac arrhythmias accompany abnormal metabolic states, auricular fibrillation in hyperthyroidism is an example of this The hypothalamus in some indirect way may be involved by virtue of the role it plays in maintaining metabolic states but this again has yet no basis in fact

Through changes in respiration Disturbances of cardiac rhythm associated with changes in the respiratory center are a matter of common observation The hypothalamus, as we have observed is related to metabolic processes and for this reason perhaps influences the respiratory center

BIBLIOGRAPHY

[1] ADRIAN E D The impulse produced by sensory nerve endings J Physiol 1926 *61* 49

[2] ANREP G V AND STACEY R S Comparative effect of various drugs upon the coronary circulation J Physiol 1927 *64* 187

[3] ANREP, G V, AND STARLING E H Central and reflex regulation of the circulation Proc Roy Soc Series B 1925 *97* 463

[4] ASCHNER B Ueber die Funktion der Hypophyse Pfluger s Arch 1912 *146* 1

[5] BAILEY P AND SWEET W H Effects on respiration blood pressure and gastric motility of stimulation of orbital surface of frontal lobe J Neurophysiol 1940 *3* 276

[6] BAINBRIDGE F A The influence of venous filling upon the rate of the heart *J Physiol* 1915 *50* 65

[7] BARD P A diencephalic mechanism for the expression of rage with special reference to the sympathetic nervous system Am J Physiol 1928 *84* 490

[8] BARD P The central representations of the sympathetic system as indicated by certain physiologic observations Arch Neurol & Psychiat 1929 *22* 230

the mechanism of the unconscious state and convul i ns studv of 3? a l litional cases Medicine 1935 14 3ii
[60] Fleisch A Venomotorenzentrum und Venenreflexe I Pflügers Arch 1930 225 26
[61] Fleisch A Venomotorenzentrum und Venenreflexe II Blutdruckzügler und Venenreflexe Pflügers Arch 1931 226 393
[62] François Franck C A Leçons sur les fonctions motrices du cerveau et sur l épilepsie cérébrale Paris Doin 1887
[63] François Franck C A Influences des excitations simples et épileptogènes du cerveau sur l appareil circulatoire Compt rend Acad d sc 1888 107 351
[64] Fulton J F Some functions of the cerebral cortex I Autonomic representation in the cerebral cortex J Michigan Med Soc 1934 33 175
[65] Fulton J F The interrelation of cerebrum and cerebellum in the regulation of somatic and autonomic functions Medicine 1936 15 247
[66] Goldenberg M and Rothberger C J Experimentelle Beiträge zur Theorie der An ina pectoris I Pitressinversuche Ztschr f d ges exper Med 1931 76 1
[67] Gollwitzer Meier, K and Krueger F Sauerstoffsverbrauch und Kranzgefäs durchblutung des innervierten Herzens in ihrer Beziehung zur Arbeit und Arbeitsform des Herzen Pflügers Arch 1938 240 263
[68] Gollwitzer Meier K and Krueger F Einfluss der Herznerven auf den Ga wechsel des Warmbluterherzens Pflügers Arch 1938 240 89
[69] Gollwitzer Meier K and Schultz H Das Verhalten der Hirn durchblutung bei Reizung der Sinusnerven Arch f exper Path u Pharmakol 1932 165 68
[70] Goltz F and Freusberg A Ueber gefasserweiternde Nerven Pflügers Arch 18 4 9 1 4
[71] Goltz F and Freusberg A Ueber d e Functionen des Len lenmarks des Hundes Pflügers Arch 18 4 8 460
[72] Goltz F Freusberg A and Gergens E Ueber gefas erweiternde Nerven Pflügers Arch 18 5 11 52
[73] Green H D and Hoff E C Effects of faradic stimulation of the cerebral cortex on limb and renal lumes in the cat and monkey Am J Physiol 1937 118 641
Grutzner P and Heidenhain R Ueber die Innervation der Muskelgefässe Pflügers Arch 18 8 16 1
[74] Gurdjian E S Webster J E and Scott F H Effect on the reflexes of the carotid sinus f ra ing the intracranial pressure Arch Int Med 1933 52 306
[75] Hartman F A Blatz W E and Kilborn L G Studies in the re eneration of denervated mammalian muscle I Volume chan e and temperature change J Physiol 1919 53 92
Hasterlik P and Biedl A Ueber die Innervation der Hautgefässe Wien klin Wchnschr 1893 6 43
[76] Hering H E Ueber die Automatie des Sau ethierherzens Pflügers Arch 190 116 143
Hering H E Der Sinus caroticus an der Ursprungsstelle der Carotis interna als Ausgang s rt eines hemmen len Herzreflexes und eines depressorischen Gefässreflexes München med Wchnschr 1924 71 01
[80] Hering H E Zur Analyse d s arteriellen Hochdrucks beim Menschen mit Hilfe des beim Karotisdruck ersuch auslosbaren drucksenkenden Gefas reflexes Münch n med Wchnschr 1925 72 333
[81] Hess W R Das Zwischenhirn und die Regulation von Kreislauf und Atmung in Beiträge zur Physiologie des Hirnstammes Leipzig Thieme 1938
[82] Hess W R Die functionelle Organization des vegetativen Nervensystems Basel Schwabe 1948
[83] Hess W R Das Zwischenhirn Basel Schwabe 1949

anatomiques et physiologiques Trav du lab de recherches biol de l Univ de Madrid 1928 *25* 331
[35] DE CASTRO F Ueber die Struktur und Innervation des Glomus caroticum beim Menschen und bei den Saugetieren Ztschr f d ges Anat Abt 1 1929 *89* 250
[36] CROUCH R AND ELLIOTT W H JR The hypothalamus as a sympathetic center Am J Physiol 1936 *115* 245
[37] CUSHING H The blood pressure reaction of acute cerebral compression illustrated by cases of intracranial hemorrhage Am J M Sc 1903 *125* 1017
[38] CUSHING H Papers relating to the pituitary body hypothalamus and parasympathetic nervous system Springfield Ill Thomas 1932
[39] CYON E AND LUDWIG, C Die Reflexe eines der sensiblen Nerven des Herzens auf die motorischen der Blutgefasse Ber ü d Verhandl d sachs Gesellsch d Wissensch Leipzig 1866 *18* 307
[40] DALE H H On some physiological actions of ergot J Physiol 1906 *34* 163
[41] DALE H H On the action of ergotoxine with special reference to the existence of sympathetic vasodilators J Physiol 1913 *46* 291
[42] DALE H H AND RICHARDS A N The vasodilator action of histamine and of some other substances J Physiol 1918 *52* 110
[43] VAN DAMME J See ref 197
[44] DANIELOPOLU D L angine de poitrine et l angine abdominale Paris Masson 1927
[45] DANILEWSKY B Experimentelle Beitrage zur Physiologie des Gehirns Pflüger s Arch 1875 *11* 128
[46] DE BURGH DALY I AND VERNEY E B Cardiovascular reflexes J Physiol 1926 *61* 268
[47] DE BURGH DALY I AND VERNEY E B The localisation of receptors involved in the reflex regulation of the heart rate J Physiol 1927 *62* 330
[48] DIKSHIT B B The production of cardiac irregularities by excitation of the hypothalamic centres J Physiol 1934 *81* 382
[49] DRESEL K Experimentelle Untersuchungen zur Anatomie und Physiologie des peripheren und zentralen vegetativen Nervensystems Ztschr f d ges exper Med 1923 *37* 373
[50] DRURY A N AND MACKENZIE D W The influence of vagal stimulation through the branches of the A V bundle in the dog J Physiol 1934 *80* 329
[51] DUSSER DE BARENNE J G AND KLEINKNECHT F Ueber den Einfluss der Reizung der Grosshirnrinde auf den allgemeinen arteriellen Blutdruck Ztschr f Biol 1924 *82* 13
[52] EPPINGER H AND WAGNER R Zur Klinik der obliterierenden Endarteritis der Lunge (primare Sklerose der Arteria pulmonalis) Wien Arch f inn Med 1920 *1* 88
[53] EULENBURG A AND LANDOIS L Die thermischen Wirkungen lokalisierter Reizung und Zerstorung der Gro hirnobe flac Vir how s Arch 1876 *68* 245
[54] EULENBURG A AND LANDOIS L Note sur l action calorifique de certaines régions du cerveau (appareils vasomoteurs situés à la surface hémisphérique) Compt rend Acad d c 1876 *82* 564
[55] VON EULER U S A vaso constrictor action of acetylcholine on the rabbit s pulmonary circulation J Physiol 1932 *74* 271
[56] EYSTER J A E AND HOOKER D R Direct and reflex response of the cardio inhibitory centre to increased blood pressure Am J Physiol 1908 *21* 373
[57] FARBER S The action of acetylcholine on the volume of the spleen of the dog Arch in ternat de pharmacodyn et de thérap 1936 *53* 367
[58] FELDBERG W Das Verhalten des Pfortaderdruckes nach Injektion von Histamin und Pepton in den Kreislauf der Katze Arch f exper Path u Pharmakol 1929 *140* 156
[59] FERRIS E B, JR CAPPS R B AND WEISS S Carotid sinus syncope and its bearing on

the mechanism of the unconscious state and convul ions stu ly of 32 ad litional cases Medicine 1935 14 3..

[a] Flei ch A Venomotorenzentrum und Venenreflexe I Pflüger s Arch 1930 225 76

[a] Fleisch A Venomotorenzentrum und Venenreflexe II Blutdruckzügler und Venenre fl xe Pflu er s Arch 1931 226 393

[a] François Franck C A Leçons sur les fonctions motrices du cerveau et sur l épilepsie cérébrale Paris Doin 1887

[a] François-Franck C A Influences des excitations imp les et épilep tog nes du cerveau sur l appareil circulatoire Compt rend Acad d sc 1888 107 351

[a] Fulton J F Some functions of the cerebral cortex I Autonomic representati n in the cerebral cortex J Michigan Me l Soc 1934 33 1..

[a] Fulton J F The interrelat on of cereb rum and cerebellum in the regulation of somatic and autonomic functions Medicine 1936 15 24.

[a] Goldenberg M and Rothberger C J Experimentelle Beiträge zur Theorie der Angina pectoris I Pitressinversuche Ztschr f d ges exper Med 1931 76 1

[a] Gollwitzer Meier K and Krueger E Sauer toffverbrauch un l Kranz efä durch blutung des innervierten Herzens in ihrer Beziehung zur Arbeit un l Arbeit form des Herzens Pflüger's Arch 1938 240 263

[a] Gollwitzer Meier K and Krueger E Einfluss der Herznerven auf den Gaswechsel des Warmbluterherzens Pfluger s Arch 1938 240 89

[a] Gollwitzer Meier K and Schulte H Das Verhalten der Hirn lurchl lutung bei Reizung der Sinusnerven Arch f exper Path u Pharmakol 1932 165 68

[a] Goltz F and Freusberg A Ueber gefasserweiternde Nerven Pfluger s Arch 1874 9 174

[a] Goltz F and Freusberg A Ueber die Functionen des Lendenmarks des Hundes Pflü ger s Arch 1874 8 460

[a] Goltz F Freusberg A and Gergens E Ueber gefä serweiternde Nerven Pflüger s Arch 1875 11 5

[a] Green H D and Hoff E C Effects of faradic stimulation f the cerebral cortex on limb and renal volumes in the cat and monkey Am J Phy iol 1937 118 641

Grutz er P and Heidenhain R Ueber die Innervati n der Mu kel ef se Pfluger s Arch 1878 16 1

[a] Guern ey C M Weisman S A and Scott F H Effect on the reflexes of the carotid sinus of raisin the intracranial pressure Arch Int Me l 1933 52 306

[a] Hartman F A Blatz W E and Kilborn L G Studies in the regeneration of denervated mammalian muscl I Volume changes and temperature changes J Physiol 1919 53 92

[a] Ha terlik P and Biedl A Ueber die Innervation der Hautgefasse Wien klin Wchn schr 1893 6 43

[a] Hering H F Ueber d e Automatie des Sau ethierherzens Pfluger s Arch 1905 116 143

[a] Hering H F Der Sinus car ticus an der Ursprungsstelle der Carotis interna als Ausgang sort eines hemmenden Herzreflexes und eines depressorischen Gefas reflexes München med Wchn chr 1924 71 01

[a] Heri g H F Zu Anal se des arteri llen Hochdrucks beim Menschen mit Hilfe des beim Karoti druc kversuch auslosbaren drucksenkenden Gefassreflexes München med Wchn schr 1925 72 339

[a] Hess W R Da Z ischenhirn und die Regulation von Kreislauf und Atmung in Beiträge zur Phys l gie des H rnstammes Leipzig Thieme 1938

[a] He W R Die functionelle Organization des vegetativen Nervensystems Basel Schwabe 1948

[a] Hess W R Das Zwischenhirn Basel Schwabe 1949

[82] HEYMANS C AND BOUCKAERT J J Le sinus carotidien zone réflexogène régulatrice du tonus des vaisseaux céphaliques Compt rend Soc de biol 1929 *100* 202

[83] HEYMANS C AND BOUCKAERT J J Sinus caroticus reflexes upon venous pressure liver volume and heart volume J Physiol 1930 *69* xxviii

[84] HEYMANS C AND BOUCKAERT J J Sinus carotidien et régulation réflexe de la circulation artérielle encéphalo bulbaire Compt rend Soc de biol 1932 *110* 996

[85] HEYMANS C AND BOUCKAERT J J Les chémo récepteurs du sinus carotidien Ergebn d Physiol 1939 *41* 28

[86] HEYMANS C BOUCKAERT J J AND DAUTREBANDE L Sinus carotidien et réflexes respiratoires II Influences respiratoires réflexes de l acidose de l alcalose de l anhydride carbonique de l ion hydrogène et de l anoxémie Sinus carotidiens et échanges respiratoires dans les poumons et au delà des poumons Arch internat de pharmacodyn et de therap 1930 *39* 400

[87] HEYMANS C BOUCKAERT J J AND DAUTREBANDE L Sinus carotidiens et modifications réflexes de la vitesse et du volume du sang circulant Compt rend Soc de biol 1931 *106* 48

[88] HEYMANS C BOUCKAERT J J AND DAUTREBANDE L Au sujet du mécanisme de la stimulation respiratoire par le sulfure de sodium Compt rend Soc de biol 1931 *106* 52

[89] HEYMANS C BOUCKAERT J J AND DAUTREBANDE L Sinus carotidien et réactions respiratoires au cyanure Compt rend Soc de biol 1931 *106* 54

[90] HEYMANS C BOUCKAERT J J AND DAUTREBANDE L Sinus carotidiens et actions stimulantes respiratoires de la nicotine et de la lobéline Compt rend Soc de biol 1931 *106* 469

[91] HEYMANS C BOUCKAERT J J AND REGNIERS P Le sinus carotidien et la zone homologue cardio aortique Paris Doin 1933

[92] HEYMANS C BOUCKAERT J J AND SAMAAN A Influence réflexe sinocarotidienne du CO_2 sur les centres cardio régulateurs Compt rend Soc de biol 1935 *118* 1246

[93] HEYMANS C AND LADON A Recherches physiologiques et pharmacologiques sur la tête isolée et le centre vague du chien I Anémie asphyxie hypertension adrénaline tonus pneumogastrique hyperthermie Arch internat de pharmacodyn et de thérap 1925 *30* 415

[94] HOFF E C AND GREEN H D Cardiovascular reaction induced by electrical stimulation of the cerebral cortex Am J Physiol 1936 *117* 411

[95] HOFF H AND URBAN H Experimentelle Studien zur Frage des essentiellen Hochdruckes Klin Wchnschr 1933 *12* 1366

[96] HOGBEN L T SCHLAPP W AND MACDONALD A D Studies of the pituitary IV Quantitative comparison of pressor activity Quart J Exper Physiol 1924 *14* 301

[97] HOLTZ P The action of pituitary posterior lobe extracts on different parts of the circulatory system J Physiol 1932 *76* 149

[98] HOUSSAY B A AND MOLINELLI E A Centre adrénalino sécréteur hypothalamique Compt rend Soc de biol 1925 *93* 1454

[99] HUME W F The action of adrenalin chloride on the human heart Quart J Med 1928 *21* 459

[100] HUNT R Vasodilator reactions I Am J Physiol 1918 *45* 197

[101] HUNT R Vasodilator reactions II Am J Physiol 1918 *45* 231

[102] HURTHLE K Die pulsatorischen Bewegungen der Aortenwand Pflüger s Arch 1935 *236* 385

[103] IKALOWICZ C AND PAL J Ueber die Kreislaufsverhaltnisse in den Unterleibsorganen Wien med Presse 1887 *28* 696

[104] DE JAEGHER, M AND VAN BOGAERT A Régulation de la tension artérielle et hypothalamus Compt rend Soc de biol 1935 *118* 544

DE JAEGHER M AND VAN BOGAERT A Hyperglycémie provoquée par excitation électrique le l hypothalamus Compt ren l Soc de biol 1935 118 1035
Kabat H Electrical stimulation of points in the forebrain and midbrain the resultant alterations in respiration J Comp Neurol 1936 64 187
KABAT H ANSON B J MAGOUN H W AND RANSON S W Stimulation of the hypothalamus with special reference to its effect on gastrointestinal motility Am J Physiol 1935 11 714
KABAT H MAGOUN H W AND RANSON S W Electrical stimulation of points in the forebrain and midbrain the resultant alterations in blood pressure Arch Neurol & Psychiat 1935 34 931
KAHLER H Ueber vasomotorische Störungen bei zerebralen Hemiplegien Wien klin Wchnschr 1922 35 219
KARPLUS J P Die Physiologie der vegetativen Zentren (Auf Grund experimenteller Erfahrungen) In Handbuch der Neurologie (Bumke & Foerster) II 402 Berlin Springer 1937
KARPLUS J P AND KREIDL A Gehirn und Sympathicus I Zwischenhirnbasis und Halssympathicus Pflugers Arch 1909 129 138
KARPLUS J P AND KREIDL A Gehirn und Sympathicus II Ein Sympathicuszentrum im Zwischenhirn Pflugers Arch 1910 135 401
KARPLUS J P AND KREIDL A Gehirn und Sympathicus III Sympathicusleitung im Gehirn und Halsmark Pfluger Arch 1911 143 109
KARPLUS J P AND KREIDL A Gehirn und Sympathicus VII Ueber Beziehungen der Hypothalamuszentren zu Blutdruck und innerer Sekretion Pflügers Arch 192 215 66
KARPLUS J P AND PECZENIK O Ueber die Beeinflussung der Hypophysentätigkeit durch die Erregung des Hypothalamus Pflugers Arch 1930 225 654
KARPLUS J P AND PECZENIK O Ueber die Beeinflussung der Hypophysentatigkeit durch Erregung des Hypothalamus II Pflugers Arch 1933 23 402
KOCH E Die reflektorische Selbststeuerung des Kreislaufes Ergebn d Kreislauff rsch 1931 1
KOCH E Die Irradiation der pressorezeptorischen Kreislaufreflexe Klin Wchnsch 1932 11 25
KOLLS A C AND GEILING E M K Contributions to the pharmacology of extracts of the posterior lobe of the pituitary gland J Pharmacol & Exper Therap 1924 24 6
KOUNTZ W B Studies on the coronary arteries of the human heart J Pharmacol & Exper Therap 1932 45 65
KROGH A The anatomy and physiology of capillaries New Haven Yale Univ Press 1929
KURÉ K Ueber den Spinalparasympathikus Basel Schwabe 1931
KURÉ K Spinalparasympathicus und Kreislauf Cardiologia 1937 1 95
KURÉ K NITTA Y TSUJI M SHIRAISHI K AND SUENAGA B Die histologische Darstellung der parasympathischen Fasern in den hinteren Rückenmarkswurzeln der Lumbalsegmente Pflugers Arch 1929 218 573
LAMPE W AND MEHES J Gefassstudien an der uberlebenden Warmbluterleber II Die Beinflussung der Lebergefasse durch Strophantin und Digitalisglykoside Arch f exper Path u Pharmakol 1926 117 1
LAMPE W AND MÉHES J Gefassstudien an der überlebenden Warmbluterleber III Die Wirkung von Hormonen auf die Lebergefasse Arch f exper Path u Pharmakol 1927 119 65
LANGLEY J N The autonomic nervous system Cambridge Heffer 1921
LESCHKE E Zur klinischen Pathologie des Zwischenhirns Deut che med Wchnschr 1920 2 959

129 LEVY A G The exciting causes of ventricular fibrillation in animals under chloroform anaesthesia Heart 1913 *4* 319
130 LEVY A G The genesis of ventricular extrasystoles under chloroform with special reference to consecutive ventricular fibrillation Heart 1914 *5* 299
131 LEVY A G Further remarks on ventricular extrasystoles and fibrillation under chloroform Heart 1919 *7* 105
132 LEWIN H AND SCHIFF F Der Einfluss der sympatischen Innervation auf die rhythmischen Erweiterungen der Kaninchenohrgefässe Pfluger s Arch 1927 *216* 657
133 MACKAY M Histamine and adrenaline in relation to the salivary secretion J Pharmacol & Exper Therap 1929 *37* 349
134 MAGOUN H W RANSON S W AND HETHERINGTON A The liberation of adrenin and sympathin induced by stimulation of the hypothalamus Am J Physiol 1937 *119* 615
136 MASSERMAN J H AND HAERTIG E W The influence of hypothalamic stimulation on intestinal activity J Neurophysiol 1938 *1* 350
137 MAUTNER H Die Bedeutung der Venen und deren Sperrvorrichtungen fur den Wasserhaushalt Wien Arch f inn Med 1923 *7* 251
138 MAUTNER H Die Innervation der Venensperre in der Leber Monatschr f Kinderh 1924 *27* 385
139 MAUTNER H Wasserbewegung im Organismus Monatschr f Kinderh 1928 *41* 78
140 MAUTNER H Austritt von Flussigkeit an der Leberoberflache Wien klin Wchnschr 1929 *42* 1290
141 MAUTNER H AND PICK E P Ueber die durch Schockgifte erzeugten Zirkulationsstorungen Munchen med Wchnschr 1915 *62* 1141
142 MAUTNER H AND PICK E P Das Verhalten der uberlebenden Leber Biochem Ztschr 1922 *127* 72
143 MAUTNER H AND PICK E P Zur Analyse der Gefasswirkung des Pituitrins Arch f exper Path u Pharmakol 1923 *97* 306
144 MAUTNER H AND PICK E P Ueber die Wirkung des Histamins auf den Kreislauf der Katze Arch f exper Path u Pharmakol 1930 *149* 25
145 MCDOWALL R J S A vago pressor reflex J Physiol 1924 *59* 41
146 MCDOWALL R J S A cardio pressor nerve J Physiol 1934 *83* 37P
147 MCDOWALL R J S The control of the circulation of the blood p 467 London Longmans Green 1938
148 MEIJLING H A Bau und Innervation von Glomus caroticum und Sinus caroticus Utrecht 1938
149 MICHAIL D AND VANCEA P L influence des zones vaso sensibles réflexogènes du sinus carotidien sur la circulation oculaire Comp rend Soc de biol 1935 *118* 469
150 MILLER H R Sclerosis of the pulmonary artery and its branches M Clin N Amer 1925 *9* 673
151 MILLER H R Clinical observations on pulmonary blood flow in silicosis and other fibrotic conditions of the lungs Am J M Sc 1936 *191* 334
152 MOISSEJEFF L Zur Kenntnis des Carotissinusreflexes Ztschr f d ges exper Med 1926 *53* 696
153 MOLITOR H AND PICK E P Die Bedeutung der Leber fur die Diurese Arch f exper Path u Pharmakol 1923 *97* 317
154 MORAT J P Les fonctions vaso motrices des racines postérieures Arch de physiol 1892 *4* 689
155 MULLER L R AND GLASER W Ueber die Innervation der Gefasse Deutsche Ztschr f Nervenh 1913 *46* 325
156 NONIDEZ J I The aortic (depressor) nerve and its associated epithelioid body the glomus aorticum Am J Anat 1935 *57* 259

Otto H L An experimental study of the extracardiac nerves Am Heart J 1928 *3* 691

Owsjannikow P Die tonischen und reflectonischen Centren der Gefassnerven Arb a d physiol Anstalt Leipzig 1872 *6* 21

Pal, J Leber die Innervation der Leber Med Jahrb 1888 *3* 67

Penfield W and Stavraky C The response of intracranial blood vessels to electrical stimulation of the thalamus and the hypothalamic regions Tr Am Neurol A 1935 *61* 144

Pike F H Personal communication

Pike F H Studies in the physiology of the central nervous system I The general phenomena of spinal shock Am J Physiol 1909 *24* 124

Pike F H Studies in the physiology of the central nervous system II The effect of repeated injuries to the spinal cord during pinal shock Am J Phy iol 1912 *30* 436

Popper L Bleibende Pulsdifferenz nach Hirnrindenläsion Deutsche med Wchnschr 1933 59 1163

Ranson S W Kabat H and Magoun H W Autonomic responses to electrical stimulation of hypothalamus preoptic region and septum Arch Neurol & Psychiat 1935 *33* 467

Ranson S W and Wightman W D Vasodilator mechanisms II The vasodilator fibers of the dorsal roots Am J Physiol 1922 *62* 392

Reed C I and Layman J A Effects of bilateral vagotomy on blood pressure and heart rate Am J Physiol 1930 *92* 215

Rein H Die Physiologie der Herz Kranzgefasse Ztschr f Biol 1931 *92* 101

Reiss M Hypophysenvorderlappen und Stoffwechselfunktion Klin Wchnschr 1939 *18* 57

Rioch D M and Brenner C Experiments on the corpus striatum and rhinencephalon J Comp Neurol 1938 68 491

Rothberger C J Beitrag zur Kenntnis der Reizleitungsstörungen nach Versuchen von Emil Zander Acta med Scandinav 1931 *75* 717

Rothberger C J and Winterberg H Ueber die experimentelle Erzeugung extrasystolischer ventrikularer Tachykardie durch Acceleransreizung Ein Beitrag zur Herzwirkung von Baryum und Calcium Pflugers Arch 1911 *142* 461

Rouget C Mémoire sur le développement la structure et les propriétés physiologiques des capillaires sanguins et lymphatiques Arch d physiol 1873 *5* 603

Rouget C Sur la contractilité des capillaires sanguins Compt rend Acad d sc 1879 88 916

Schiff M Untersuchungen zur Physiologie des Nervensystems mit Berucksichtigung der Pathologie Frankfurt am Main Rutten 1855

Schiff M Untersuchungen uber die motorischen Functionen des Grosshirns Arch f exper Path u Pharmakol 1875 3 171

Schretzenmayr A Die Motorik des intakten Venensystems I Methode der Venenokymetrie Arch f exper Path u Pharmakol 1935 *178* 731

Schretzenmayr A Die Motorik des intakten Venensystems II Nachweis und Bedeutung der Wellvenenmotorik Arch f exper Path u Pharmakol 1936 *187* 295

Schrottenbach H Beitrage zur Kenntnis der Uebertragung vasovegetativer Funktionen im Zwischenhirn I II Ztschr f d ges Neurol u Psychiat 1914 *23* 431 497

Schrottenbach H Beitrage zur Kenntnis der Uebertragung vasovegetativer Funktionen im Zwischenhirn III IV Ztschr f d ges Neurol u Psychiat 1916 *33* 229

Schurmeyer A Leber die Innervation der Pars intermedia der Hypophyse der Amphibien Klin Wchnschr 1926 *5* 2311

Scott J M D and Roberts F The localisation of the vasomotor centre J Physiol 1923 *58* 168

183 SILVER, G A, AND MORTON H G The central action of acetylcholine J Pharmacol & Exper Therap 1936 *56* 446

184 SPIEGEL E A Experimentelle Analyse der vegetativen Reflexwirkungen des Labyrinths In Handbuch der Neurologie des Ohres III 631 Berlin Urban 1926

185 SPIEGEL E A AND SAITO S Ueber die hormonale Erregbarkeit vegetativer Zentren Arb a d neurol Inst a d Wien Univ 1924 *25* 247

186 SPIEGEL E A AND YASKIN J C Untersuchungen am zentralen vasomotoren Apparat Ztschr f d ges exper Med 1928 *63* 505

187 STRICKER S Untersuchungen über die Gefassnerven Wurzeln des Ischiadicus Sitzungsb Akad d Wissench Wien Math natur Kl III Abt 1876 *74* 173

188 STRICKER S Entgegnung auf die Mitteilung des Herrn Vulpian Ueber die Gefassnerven in den sensiblen Ruckenmarkswurzeln Med Jahrb 1878 *8* 409

189 STRICKER S Untersuchungen über Contractilitat der Capillaren Sitzungsb d Akad d Wissensch Wien Math natur Kl III Abt 1876 *74* 313

190 SUH T H WANG C H AND LINN R K S The effect of intracisternal applications of acetylcholine and the localization of pressor centre and tract Chinese J Physiol 1936 *10* 61

191 TELLO J F Développement et terminaison du nerf depresseur Trav du lab de recherches *biol de l Univ de Madrid 1924 22 219*

192 TIGERSTEDT R A A Die Physiologie des Kreislaufes Berlin de Gruyter 1923

193 VAN BOGAERT A Modifications de la fréquence du rythme et du volume systolique du coeur par excitation hypothalamique Compt rend Soc de biol 1935 *119* 1240

194 VAN BOGAERT A Action des extraits de l hypophyse sur le diencéphale et sur la tension artérielle Compt rend Soc de biol 1935 *120* 450

195 VAN BOGAERT A Hypotension artérielle expérimentale d origine centrale Compt rend Soc de biol 1935 *120* 1043

196 VAN BOGAERT A Hypothalamus et réactions cardio vasculaires d origine centrale Arch internat de pharmacodyn et de thérap 1936 *53* 137

197 VAN DAMME J Sensibilité reflexogène de la région de la bifurcation carotidienne du mouton vis a vis des modifications de pression et des substances chimiques Compt rend Soc de biol 1933 *113* 909

198 VERWORN M Zur Analyse der dyspnoischen Vagusreizung Arch f Anat u Physiol Physiol Abt 1903 65

199 VERZÁR F AND PÉTER I Die tonische Erregungsvorgang im N vagus Pfluger s Arch 1926 *212* 24

200 WALLENBERG A Notiz uber einen Schleifenursprung des Pedunculus corporis mammillaris beim Kaninchen Anat Anz 1899 *16* 156

201 WALLENBERG A *Bemerkenswerte Endstatten der Grosshirnfaserung bei* Saugern Jahrb f Psychiat u Neurol 1934 *51* 295

202 WANG G AND RICHTER C Action currents from the pad of the cat s foot produced by stimulation of the tuber cinereum Chinese J Physiol 1928 *2* 279

203 WATERMAN L Over de vasomotorische beteekenis der groote hersenen Nederl tijd chr v geneesk 1935 *31* 3806

204 WATTS J W AND FULTON J F The effect of lesions of the hypothalamus upon the gastro intestinal tract and heart in monkeys Ann Surg 1935 *101* 363

205 WERZILOFF N M Zur Frage uber die vasomotorische Function der hinteren Wurzeln Centralbl f Physiol 1896 *10* 194

206 WIGGERS C J Physiology in health and disease Philadelphia Lea & Febiger 1934

207 WINKLER F Die zerebrale Beeinflussung der Schweissekretion Pfluger s Arch 1908 *125* 584

208 WOOLLARD H H The innervation of the heart J Anat 1926 *60* 345

SECTION THREE

Autonomic Pathways for Cardiac Pain

CHAPTER VI

Peripheral Pathways for General Autonomic Reactions*

Reaching into every recess of the body and consisting of an extensive interconnected system of ganglia and nerves the autonomic nervous system is characterized particularly by the formation of plexuses a feature absent in the somatic nervous system All the smooth muscles and glandular epithelium of the body receive autonomic nerves A minor supply goes to the striated (voluntary) skeletal muscles according to Boeke[2, 3] but Hinsey[4] appears to have shown that skeletal muscles are not innervated by sympathetic fibers The chief and predominant innervation of these muscles however is through the cerebrospinal system The viscera on the other hand are supplied wholly by autonomic fibers the largest part of the entire autonomic system consisting of visceral nerves

An autonomic efferent fiber has its cell body within the neuraxis These cells are grouped as follows in the pars intermedia of the gray *matter for the sym*pathetic system and the sacral autonomics in the rhombencephalon and midbrain for the cranial autonomics Differing from afferent fibers as well as from somatic neurons autonomic efferent fibers whether sympathetic or parasympathetic always undergo interruption in a ganglion Central to the point of intraganglionic interruption or relay the neuron is designated as preganglionic it is medullated (white) Some of the splanchnic nerves which are unmyelinated and some preganglionic vagal fibers are minor exceptions to this rule Distal to the intraganglionic relay the neuron now termed postganglionic down to its termination is unmedullated (gray) some neurons as is the case of the finely medullated postganglionic fibers leaving the ciliary ganglion are white (Spiegel[14])

The large numbers of afferent and efferent fibers make up two separate divisions of the autonomic system a sympathetic orthosympathetic or thoracolumbar system and a parasympathetic or craniosacral system

* Diagrams illustrations etc of the peripheral autonomic nervous system have not been included since they are available in many textbooks and atlases on general anatomy and neurology

Sympathetic Efferent (Centrifugal) Fibers*

Preganglionic Neurons The neurons originate in cells of the gray matter of the pars intermedia, these cells forming a single continuous column from C 8 to L 3 The preganglionic fibers emerge in the ventral roots of spinal nerves, then pass through white rami at corresponding levels and reach corresponding ganglia in the sympathetic paravertebral trunk The trunk or ganglionated chain, containing afferent and efferent fibers is marked off into cervical thoracic, lumbar, and sacral divisions, there is one coccygeal ganglion Most of the cervical and lumbar roots have no white rami and obviously no preganglionic fibers

Lying on each side of and ventral to the bodies of the vertebra are the vertebral ganglia termed also central (ventral) ganglia The paravertebral (also called collateral) ganglia are found at a distance from the main ganglionated chain, more in the mid line, in the abdominal and thoracic cavities these ganglia are close to various plexuses

Each neuron in the main ganglionated trunk pursues one of three courses (1) it terminates in a vertebral ganglion corresponding to the level of its emergence, (2) it travels up or down in the vertebral ganglionated trunk, arborizing with dendrites of a ganglionic cell in a higher or lower ganglia, or (3) it traverses the ganglion corresponding to the level of its emergence and still unbroken, reaches a subsidiary collateral or paravertebral ganglion well beyond the ganglionated trunk The stream of preganglionic fibers leaving the neuraxis receives *practically no contribution from the cervical or lower lumbar segments of the* spinal cord, there are therefore, no white rami at these levels

The relationship of preganglionic to postganglionic neurons is important Langley[8-10] demonstrated that not all preganglionic fibers coursing through a single white ramus are destined for one sympathetic segmental ganglion on the contrary, fibers from one level pass to a series of about six to nine ganglia Moreover, a single preganglionic neuron has dendritic connections with many postganglionic axons (Bidder and Volkmann[1]) According to Ranson and Billingsley,[1] in the superior sympathetic cervical ganglion of the cat each preganglionic neuron is *in synaptic junction* with about thirty two postganglionic neurons This seems to be an adaptation whereby a single efferent impulse is able to touch off a multitude of peripheral reactions and is probably the basis for "autonomic irradiation " a term used by Schweitzer[13] after Kisch[6] to denote the wide and varied autonomic effects which stem from the neuraxis

Postganglionic Neurons Leaving the ganglion wherein a synaptic connection takes place the postganglionic neuron courses through a gray communicating ramus at a corresponding level and then passes by way of a spinal somatic nerve either to the periphery or by way of a visceral sympathetic nerve to a viscus The function of these post ganglionic fibers is not the same for all organs The regional *distribution of this fiber system* is depicted in Figure 12

* Consult Chapter IV for regional distribution of sympathetic innervations

Sympathetic Afferent (Centripetal) Fibers

The afferent neurons a large and diffuse group transmit sensory impulses from various structures and organs into the central nervous system These fibers participate in the reflex nervous arc which connects well defined districts of the outer integument (dermatomes) to corresponding segmental levels of the cord Unlike the efferent neurons these are without a relay for example a neuron travels directly from a viscus into the neuraxis and in so doing passes uninterruptedly through a sympathetic ganglion Traversing the ganglion the neuron continues its way within a white communicating ramus at a corresponding level and in this manner reaches a spinal dorsal ganglion on the posterior root of a spinal nerve corresponding to the level of the white ramus The cell body of origin of each neuron is in the dorsal ganglion from this cell body a central axon goes into the substantia gelatinosa of the spinal cord and establishes a synaptic contact with the spinothalamic tract or goes to the anterolateral portion of the gray matter in the cord to connect with efferent neurons at the same or adjoining levels

The absence of any relay in afferent sympathetic fibers has raised the question whether these fibers are truly part of the sympathetic system Furthermore certain physiologic and pharmacologic features of these neurons seem to place them outside or at least apart from the sympathetic efferent system of neurons The afferent system conveys sensory impulses through the spinal cord to the higher brain centers and this system of fibers is distinguished anatomically by a predominance of spinal entry with reference to any viscus Thus afferent neurons better termed visceral fibers when they innervate a viscus have a concentrated zone of entry into the cord for example at Th 1 to 4 on the left side from the heart Like all other organs however the heart is connected to other spinal cord levels by accessory afferent fibers

Accessory fibers may participate in the propagation of sensory impulses (pain) into multiple segments of the spinal cord or under certain circumstances they may take over the main burden of conduction The general pattern of a preponderance of entry plus the arrangement of accessory fibers which gain an entry into the cord is a fundamental anatomic endowment exhibiting important variations however in some mammals including man In individuals with such variations from the norm the afferent innervations may exist as a system of very diffuse fibers coming from widely separated organs and overlapping within common receptor levels in the spinal cord

Parasympathetic Efferent (Centrifugal) Fibers*

Almost as widely distributed as the sympathetic the parasympathetic division has a more limited origin in the cerebrospinal system It too contains efferent and afferent fibers Each efferent (centrifugal) fiber has a preganglionic and postganglionic component separated by a synapsis within a parasympathetic ganglion

* Consult Chapter IV for regional distribution of parasympathetic innervations

Preganglionic Neurons These arise in cell bodies grouped as isolated clusters or aggregations, not as a continuous column Practically all these neurons are medullated, although some vagal fibers have no myelin sheaths The preganglionic neurons have several levels of emergence

1 A midbrain outflow includes fibers in the third cranial nerve for the ciliary ganglion

2 A rhombencephalic group Of these one set travels as the intermediate or Wrisberg's nerve to form the chorda tympani, the tympanic nerves joins the lingual nerve which ends in the submaxillary ganglion Another set of fibers travels with the facial nerve and forms the great superficial petrosal nerve (the motor part of the Vidian nerve) which ends in the sphenopalatine ganglion A third set joins the ninth cranial nerve and forms the tympanic nerve (Jacobson's nerve) and then forms the lesser superficial petrosal nerve ending in the otic ganglion A fourth set consists of the vagus with its wide distribution of fibers to ganglionic cells lying in the walls of organs innervated by this large nerve system

3 The sacral outflow carries preganglionic fibers in the anterior rami of the second, third, and fourth sacral nerves These nerves run to the ganglia in the pelvic plexuses or to the ganglia in the pelvic organs

4 The so called posterior root outflow (Kure[7])

Postganglionic Neurons As a rule, these neurons are unmedullated although the fibers leaving the ciliary ganglion are medullated As in the case of the preganglionic neurons the postganglionic also make up several groups

1 The midbrain outflow leaves the ciliary body and supplies the pupillary sphincter and the ciliary muscles of the eyeball

2 The rhombencephalic outflow contains the following subdivisions Fibers from the submaxillary ganglion go to the submaxillary and sublingual glands Fibers from the sphenopalatine ganglion go to the lachrymal glands and to the glands in the mouth and nose Fibers from the otic ganglion go to the parotid gland Fibers from the ganglion cells of the vagus system form an extensive innervation to the chest abdomen and other parts, providing inhibitory neurons to the myocardium vasoconstrictors to the coronaries vasodilators to the pulmonary vessels constrictors to the bronchial musculature motor and secretory neurons respectively to the smooth muscles and glands of the alimentary tract down to the ileocolic valve and visceral fibers to the liver, pancreas, kidneys, adrenals

3 The postganglionic fibers of the sacral division leave the ganglia of plexuses in this region and supply fibers to the distal colon rectum, and the genito urinary organs

4 A fourth division recently the subject of special study by Kure, is to be found in the so called posterior root outflow This division is supposed to contain parasympathetic fibers However, the support for the contention that these fibers are parasympathetic is largely if not wholly, indirect and is based

on the fact that these fibers behave in a way analogous to that which characterizes parasympathetic fibers namely, they are cholinergic in function and the injection of acetylcholine brings on responses identical with those induced by electrical excitation of these fibers Another argument advanced for grouping these fibers as parasympathetic rests on the fact that vasodilation in certain regions of the body is known to be parasympathetic for example the effect noted on stimulating the chorda tympani Kahr and Sheehan[9] have offered histologic proof of the existence of efferent fibers in the posterior spinal roots and Matthews[11] on the basis of action currents supports these findings

The alleged existence of a supply of parasympathetic postganglionic neurons to the periphery namely to blood vessels sweat glands and pilo-erector muscles is not well founded on anatomic evidence

Parasympathetic Afferent (Centripetal) Fibers

Elsewhere (p 169) we have suggested that although the vagal fibers seem to transmit sensory impulses from the bronchial and gastro-intestinal musculature the parasympathetic afferent innervation probably may not be a true conductor of pain at least from the heart In the third and seventh cranial nerves afferent parasympathetic fibers have not been demonstrated In the vagus nerve afferent fibers from peripheral nerve endings travel to cells within the trunk ganglia (jugular and nodosal) and from these cells of origin central axons penetrate the medulla and reach the lateral part of the dorsal nucleus of the vagus (This will be recognized as a general arrangement similar to that already noted in connection with the dorsal spinal ganglion for afferent sympathetic fibers) Afferent vagal fibers arise from the ascending aorta and the heart also from the lungs the bronchial system the abdominal viscera stomach small gut proximal colon liver spleen pancreas kidneys and adrenals They are also found within the pelvic nerves related to the sacral levels of the cord

A double innervation sympathetic and parasympathetic supplies the majority of internal organs There are however some exceptions In certain peripheral structures a dual autonomic set of reactions operate through a single division of the autonomic innervations for example cutaneous blood vessels are able to dilate or contract by means of their sympathetic supplies, and similar observations have been made with respect to the salivary glands and uterine muscles The reaction of the latter is influenced by their state of contraction or relaxation and by conditions bound up with the virginity of the animal

BIBLIOGRAPHY

Bidder F H and Volkmann A W Die Selbstandigkeit des sympathischen Nervensystems durch anatomische Untersuchung nachgewiesen Leipzig Breitkopf & Härtel 1842

[2] Boeke J Die motorische Endplatte bei den hoheren Vertebraten Anat Anz 1909 35 193

[3] BOEKE, J Die doppelte efferente Innervation der quergestreiften Muskelfasern Anat Anz 1913 *44* 343

[4] HINSEY J C Some observations on the innervation of skeletal muscle of the cat J Comp Neurol 1927 *44* 87

[5] KAHR S AND SHEEHAN D The presence of afferent fibers in posterior spinal roots Brain 1933 *56* 265

[6] KISCH B Die irradiation autonomer Reflexe und ihre Beziehung zu gewissen patholo ısch phy iologischen Erscheinungen Ztschr f d ges exper Med 1926 *52* 499

[7] KURÉ K Spinal parasympathetics Quart J Exper Physiol 1931 *21* 1

[8] LANGLEY J N Notes on the cervical sympathetic and chiefly on its vasomotor fibers J Physiol 1893 *14* 2

[9] LANGLEY J N The autonomic nervous system Brain 1903 *26* 1

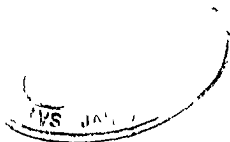
[10] LANGLEY J N The autonomic nervous system Cambridge Heffer 1921

[11] MATTHEWS B H C Impulses leaving the spinal cord by dorsal nerve roots J Physiol 1934 *81* xxix

[12] RANSON S W AND BILLINGSLEY P R Studies on the sympathetic nervous system J Comp Neurol 1918 *29* 359

[13] SCHWEITZER A Die irradiation autonomer Reflexe Basel S Karger 1937

[14] SPIEGEL E A The autonomic nervous system In Practice of Pediatrics Ed by J Brennemann IV chap 19 Hagerstown Md Prior 1937



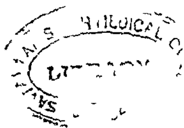
CHAPTER VII

The Sympathetic Pathways for Anginal Pain

An introductory group of five drawings is presented to help the reader in general orientation. This is followed by a progressive series of drawings designed to depict step by step the sympathetic cardiac innervations which bear upon the clinical and physiological problems which go to make up the main theme of this volume.

The practical division of the cardiac sympathetics into afferent and efferent groups draws special interest to the question of whether the afferent fibers are truly part of the sympathetic apparatus. Attention has been paid to this problem in this text but of greater significance is the fact that the afferent fibers unquestionably conduct sensory impulses from the heart into the neuraxis. Of equal import is the circumstance that cardiac pain may enter the neuraxis by accessory afferent routes and that, conversely, the cardiac apparatus may be the recipient of pain which travels along extracardiac afferent pathways. These considerations, it is hoped, will take on an increased practical value as the reader becomes familiar with anatomic details. A similar familiarization with respect to the vagal supplies and the dermatomic innervations *set forth in* Chapters VIII, IX and X will complement the information obtained in Chapter VII.

This entire section, dealing with the autonomic pathways for pain has been planned to give the student an enlarged basis for understanding the clinical *significance* of the varying aspects of anginal pain *and allied manifestations*. For those unfamiliar with the anatomic details it is suggested that particular attention should be paid to the legends and their *corresponding figures*. To help concentrate on these physiologic as well as clinical aspects have, as far as possible, been omitted from this section.



[3] BOEKE, J Die doppelte efferente Innervation der quergestreiften Muskelfasern Anat. Anz 1913 *44* 343

[4] HINSEY J C Some observations on the innervation of skeletal muscle of the cat J Comp Neurol 1927 *44* 87

[5] KAHR S AND SHEEHAN D The presence of afferent fibers in posterior spinal roots Brain 1933 *56* 265

[6] KISCH B Die irradiation autonomer Reflexe und ihre Beziehung zu gewissen pathologisch physiologischen Erscheinungen Ztschr f d ges exper Med 1926 *52* 499

[7] KURÉ K Spinal parasympathetics Quart J Exper Physiol 1931 *21* 1

[8] LANGLEY J N Notes on the cervical sympathetic and chiefly on its vasomotor fibers J Physiol 1893 *14* 2

[9] LANGLEY J N The autonomic nervous system Brain 1903 *26* 1

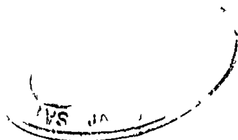
[10] LANGLEY J N The autonomic nervous system Cambridge Heffer 1921

[11] MATTHEWS B H C Impulses leaving the spinal cord by dorsal nerve roots J Physiol 1934 *81* xxix

[12] RANSON S W AND BILLINGSLEY P R Studies on the sympathetic nervous system J Comp Neurol 1918 *29* 359

[13] SCHWEITZER A Die irradiation autonomer Reflexe Basel S Karger 1937

[14] SPIEGEL E A The autonomic nervous system In Practice of Pediatrics Ed by J Brennemann IV chap 19 Hagerstown Md Prior 1932



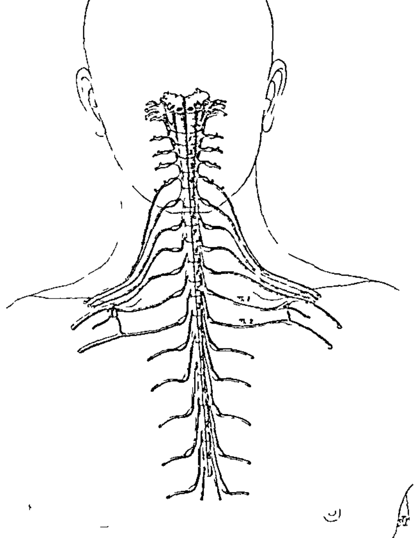


Fig 26 The Spinal Cord and the Emergence of the Spinal Nerves at Their Respective Cord Levels For the sake of simplicity the anterior nerve roots have been omitted Observe that although there are but seven cervical vertebral bones there are eight cervical spinal cord segments from each of which a pair of spinal nerves emerges Note also the bundle of nerve strands (the brachial plexus) formed by the confluence of the 4th 5th 6th 7th 8th cervical nerves and the 1st thoracic This is the so-called prefixed brachial plexus In some individuals the plexus is shifted downward one cord level beginning with the 5th cervical nerve and ending with the second thoracic nerve This is called the postfixed plexus.

Brachial plexus fibres go to each side of the neck down each arm and over part of the pectoral areas In connection with cardiac disorders two points deserve special emphasis (1) the left brachial plexus practically always is the one involved and (2) as a rule only a particular portion of the plexus carries anginal pain namely the portion limited to the first and second thoracic nerves.

The drawing of the left brachial plexus has been extended toward the arm in order to show the manner in which the left first and second thoracic nerves pass into the plexus

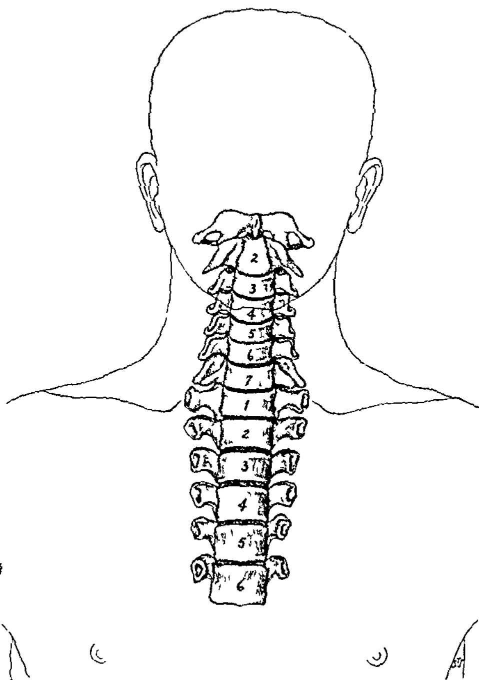


FIG 25 The Vertebrae This drawing shows the vertebral bones from the base of the skull to the eighth thoracic level inclusive

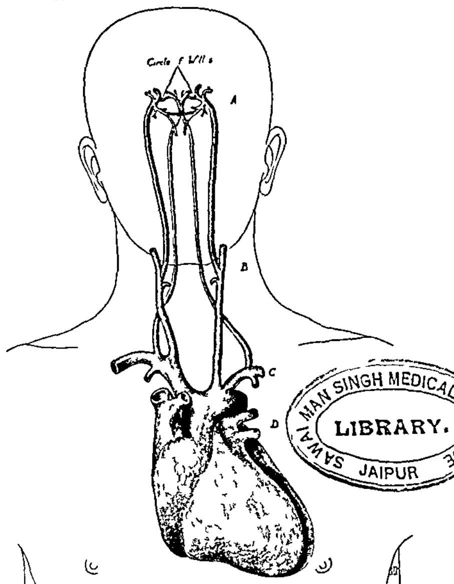


Fig 28 The Heart and the Arterial Tree from the Heart to the Circle of Willis in the Brain In order to facilitate the localization of special portions of the cardiac nerve supply several levels are designated on this vascular tree at points of vessel bifurcation as a rule These levels are A at the circle of Willis B at the point of bifurcation of the common carotid artery C at the subclavian artery at the emergence of the vertebral artery and D at the bifurcation of the pulmonary artery

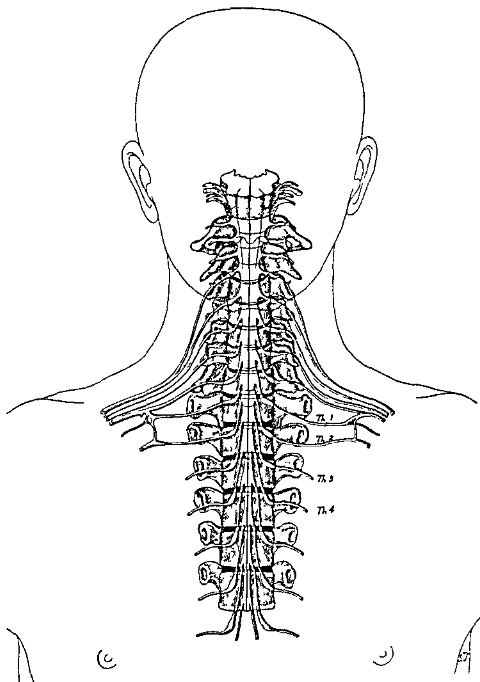


FIG 27 The Two Preceding Drawings 1 and 2 Are Superimposed The vertical bone levels are seen to lie slightly below their corresponding cord segments Because of this each spinal nerve emerges through an intervertebral foramen at a level below its point of origin

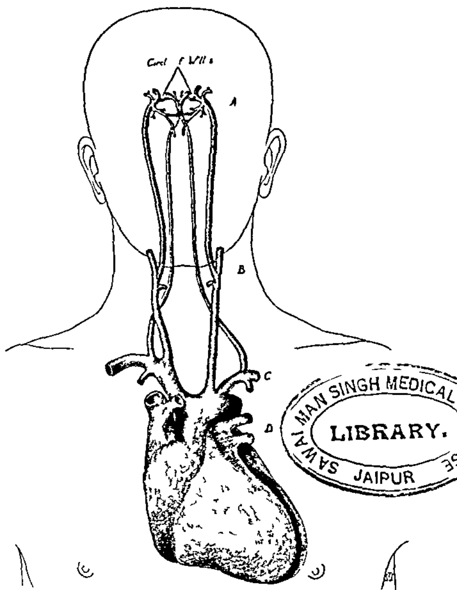


Fig 28 The Heart and the Arterial Tree from the Heart to the Circle of Willis in the Brain In order to facilitate the localization of special portions of the cardiac nerve supply several levels are designated on this vascular tree at points of vessel bifurcation as a rule These levels are *A* at the circle of Willis *B* at the point of bifurcation of the common carotid artery C at the subclavian artery at the emergence of the vertebral artery and *D* at the bifurcation of the pulmonary artery

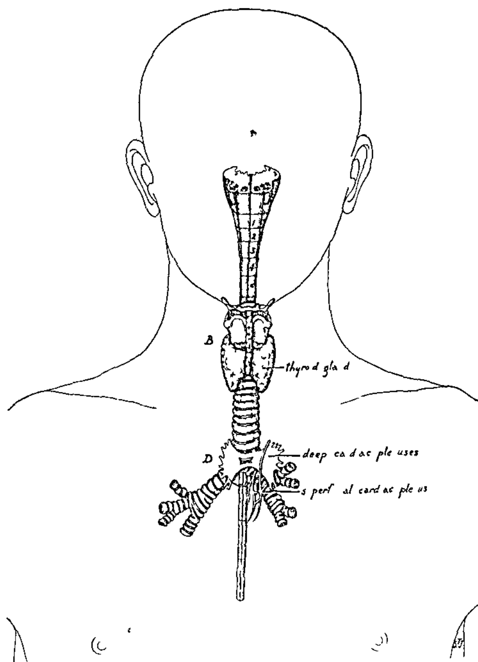


Fig 29 The Thyroid Gland at Level *B* and the Cardiac Plexuses at Level *D* The thyroid gland is at level *B* a region of convergence for many sympathetic and vagal fibres The superficial and deep cardiac plexuses lie at level *D* There is only one superficial cardiac plexus and it rests in the concavity of the aortic arch in front of the bifurcation of the left pulmonary artery There are two deep cardiac plexuses each is behind the aortic arch on either side of the trachea just above its bifurcation considerably larger than the superficial plexus (For the cardiac plexuses and relations to other plexuses see Fig 40 p 163)

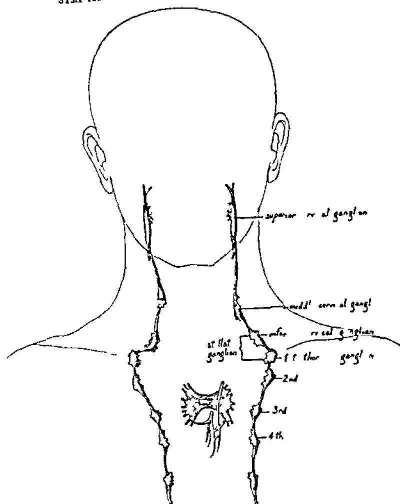


FIG 30 The Sympathetic Cardiac Innervation This is the first of a series of drawings to illu trat the mpathetic component of the cardiac innervation It is part of the large sympathetic d vi ion that supplies the rest of the body and this division together with the para sympath tic (r cranio-sacral) division forms the autonomic nervous system for the entire body As in other organs this dual innervation exists in the case of the cardiovascular struc t es A descrij t on of the parasympathetic or vagal system will follow later (Chapter VIII)

The cervical t nk and ganglia The upper or cervical part of the sympathetic supply to the heart consists of a bilateral longitu linal sympathetic trunk in which three cervical ganglia and

four sometimes five thoracic ganglia stand out on each side This ganglionated trunk is behind the carotid sheath The three cervical ganglia represent the fusion of eight ganglia the superior ganglion is the fusion of four, the middle of two and the inferior of two

The superior cervical ganglion is about two to three cm long and oval or fusiform in shape It lies in front of the transverse processes of the second and third cervical vertebrae and behind the upper portion of the sheath of the great vessels of the neck Sometimes it is double or split so that one portion may lie before and another behind the carotid sheath sympathetic filaments bridging the gap

The middle cervical ganglion is smaller tends to be triangular in outline and is sometimes absent Its position is variable but it is usually found at the level of the transverse portion of the sixth cervical vertebra i e about the level of the cricoid cartilage anterior to the bend of the inferior thyroid artery

The inferior cervical ganglion larger than the middle and irregular in shape is found deeper in the neck at the level of the transverse process of the seventh cervical vertebra lateral to its body and anterior to the neck of the first rib and posterior to the vertebral or the first portion of the subclavian artery It is important to recognize that this large ganglion is directly blended with (or else connected by a short stout trunk to) the first thoracic ganglion The combination of these two is known as the stellate ganglion

The thoracic trunk and ganglia There are ten or eleven ganglia in this thoracic trunk but only the upper four or five are commonly concerned with anginal pain The ganglia are smaller than the cervical they are irregularly angular or fusiform in shape joined by a common cord or *trunk quite thick These upper ganglia are united to the corresponding thoracic* spinal nerves on each side Each nerve excluding possibly the first has a *visceral* branch the white ramus which connects it with the corresponding sympathetic thoracic ganglion The upper four or five white rami are important bridges as we shall see

The second thoracic nerve usually communicates with the first thoracic nerve

The cardiac plexuses (See Fig 40 p 163)

Not all the structures mentioned above are featured in this drawing They are described however in order to give the reader some idea of their dimensional relationship This will be clearer with the development of other drawings



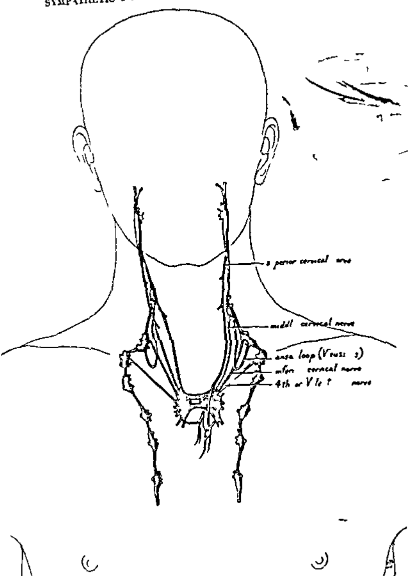


FIG 31 The Cardiac Nerves Between the Sympathetic Cervical Ganglia and the Cardiac Plexuses The superior middle and inferior cardiac nerves act as direct longitudinal strands for the transmission of impulses between the cervical sympathetic gan lia and the cardiac plexuses Each ganglion sends a nerve to the deep cardiac plexus of the same side with the exception of the left superior cervical ganglion whose nerve enters the superficial cardiac plexus situated on the left side

The superior nerve crosses the inferior thyroid artery on its dorsal aspect and before reaching the cardiac plexus runs toward the innominate artery on the right side and the common

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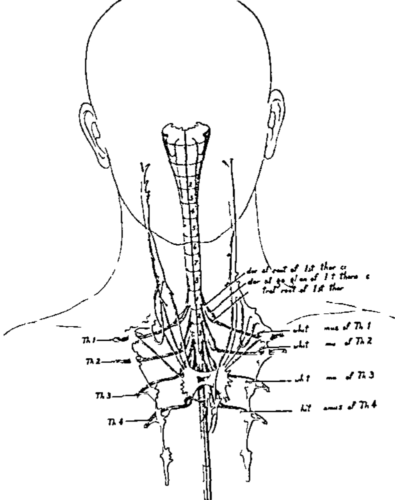


Fig 32 The Anterior and Posterior Divisions of the Spinal Thoracic Nerves The anterior and posterior divisions of the upper four or five thoracic spinal nerves are depicted On each posterior division close to its entry into the cord lies a root ganglion The sympathetic fibres that enter the neuraxis pass through these upper four or five posterior divisions and their respective spinal root ganglia The bulk of afferent sympathetic fibres from the heart and aorta takes this course

B The Communicating White Rami Four (or five) white rami running as transverse bridges connect the corresponding four (or five) thoracic ganglia to corresponding segments in the spinal cord These rami carry afferent fibres (they also carry efferent fibres) which enter the spinal root ganglion of the posterior division of each thoracic nerve each root ganglion lies close to the cord Since there are no white rami above the level of the first thoracic sympathetic ganglion impulses above this level destined for the central nervous system must descend it is claimed to this level before crossing into the cord

carotid artery on the left side On each side the nerve finds an anastomosis with the superior cardiac branches of the vagus and with both laryngeal nerves Sometimes a smaller special ganglion the superior cardiac ganglion appears along the course of this nerve below the point of crossing of the inferior thyroid artery At its points of entry into the cardiac plexus the left superior cardiac nerve contains another small ganglion (ganglion of Wrisberg or magnum) the ganglion is sometimes divided This nerve may be lacking on one side and even on both sides

The middle magnus nerve and the middle sympathetic ganglion as well may be absent the nerve arising from the trunk at about the site where the latter crosses the inferior thyroid artery The nerve anastomoses with the recurrent laryngeal nerve (vagus) and reaches the subclavian artery Below the thoracic aperture level the nerve occasionally has a ganglion of its own the middle cardiac ganglion

The inferior or small sympathetic nerve leaves the inferior cervical sympathetic ganglion (or stellate ganglion formed by the lowermost cervical and the first thoracic ganglia) As it continues downward on the right side it lies behind the innominate artery on the left side behind the aortic arch The nerve on each side anastomoses with the recurrent laryngeal nerve it joins with the middle or magnus nerve to form the nervus cardiacus crassus

Another nerve is sometimes present a fourth or accessory sympathetic cardiac nerve the nerve of Valentine or nerve imus it goes to the deep cardiac plexus The nerve is given off by the first thoracic ganglionic component of the stellate ganglion

A special strand or loop the ansa Vieussens connects the middle and the stellate ganglia This loop is clearly seen at the level of the emergence of the vertebral artery from the subclavian artery (see Fig 34 Insert A, p 149)

Some anatomists Schuhmacher[22] for instance claim that the sympathetic fibres from the right side supply the right heart the left sympathetic fibres the left heart

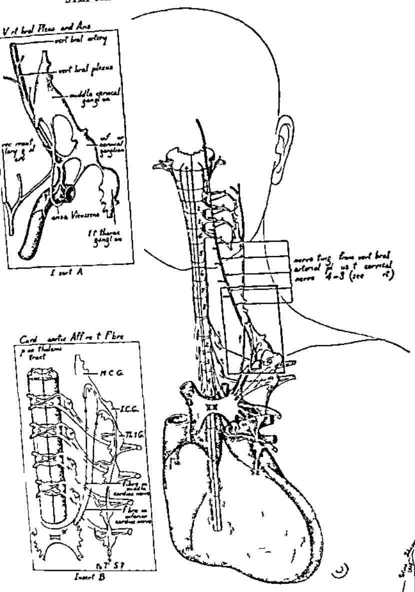


Fig 34 The Afferent Sympathetic Cardiac Fibres

Fig 34 The Afferent Sympathetic Cardiac Fibres The course of an impulse in the sympathetic system from the cardiac plexuses to the brain will now be traced

It is controversial whether impulses from the superficial cardiac plexus ascend along the upper r ca diac nerve the weight of evidence i against the existence of afferent fibres in this nerv Impulses from the deep cardiac plexus however ascend along the middle and

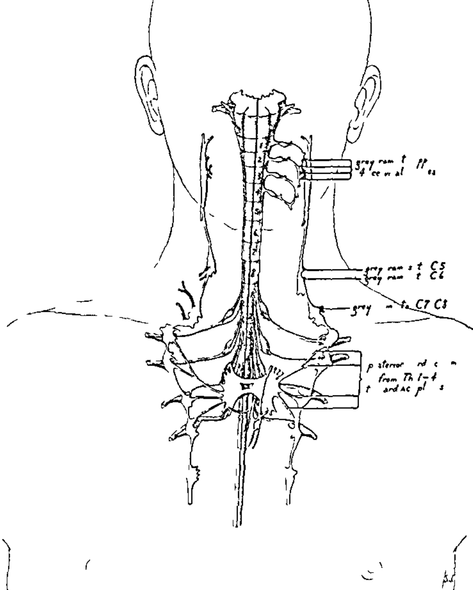
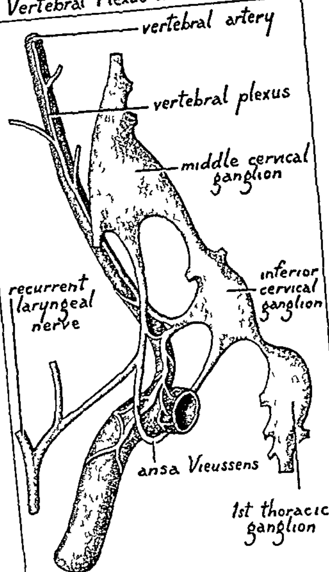


FIG 33 The Posterior Sympathetic Cardiac Fibres A recently discovered set of grey rami on each side travels from the cardiac and pulmonary plexuses backward through the posterior mediastinum to the 2nd 3rd and 4th occasionally the 1st and the 5th and 6th thoracic sympathetic ganglia (See lateral view Fig 37 p 158) These rami represent an anatomic bridge between the upper thoracic sympathetic chain and the pulmonary and cardiac plexuses As in the case of the white rami they are absent in the cervical region These posterior rami have been demonstrated by Jonesco and Enachesco [11] by Brauecker [2] by Kuntz[13, 14] Cannon Lewis and Britton [5] Mixter and White [15] also Singer and Spiegel[23] have written of their significance It is claimed that these rami contain afferent and efferent fibres from the heart and aorta to the central nervous system

The Communicating Grey Rami A different set of rami is depicted here the grey rami in the cervical and upper thoracic regions The cervical are arranged four rami arising from the superior cervical ganglion two from the middle three from the stellate The thoracic rami emerge from each ganglion by either one or two strands From each ganglion the ramus or rami pass into the posterior division of the corresponding thoracic spinal nerves These arrangements are very much the same on each side



Insert A

Fig 34 Insert A Vertebral Plexus and Ansa

Fig 34 Insert A a *The sympathetic vertebral network* The stellate ganglion or better its first thoracic component gives off the vertebral nerve which forms a network plexus around the vertebral artery Beginning at the origin of this vessel from the subclavian artery and extending upward to the skull the network or plexus in its course sends connecting branches to the 5th 6th 7th (in lower mammals the 8th also) cervical nerves very rarely to the 4th The plexus is quite variable in the dog cat fox and horse but in man comparatively more constant By some authorities notably Danielopolu the plexus is looked upon as a separate deep communicating system from the stellate ganglion to the lower cervical nerves in contrast to the more superficially placed communicating system that traverses the distance between all three cervical sympathetic ganglia and the 8th cervical and 1st thoracic nerves.

inferior cardiac nerves to their respective cervical sympathetic ganglia To reach the brain from these ganglia several possible routes lie open

1 The best understood and by all means the most probable pathway continues from these ganglia down the sympathetic trunk to the levels between the first and the fourth thoracic ganglion ometimes the fifth From this region fibres pass across the corresponding four or five communicating loops the white rami Each of these rami carries afferent fibres into a corresponding thoracic spinal dorsal root ganglion lying on a posterior division of a thoracic nerve The afferent nerve filament that begins in a portion of the heart for example and passes through the cardiac plexus to reach a cell in the posterior root ganglion is but the peripheral process of that cell The central process or fibre of this cell enters the spinal cord through the proximal portion of the posterior root nerve and has its ending in the posterior horn of the grey matter the substantia gelatinosa Rolandii In the grey matter the central fibre comes into contact with the fibres of the spinothalamic tract thus forming its first and as far as we know its only synaptic connection The synapsis is not altogether well defined (see insert A Fi 34 p 151)

2 A second possible route to the brain leads through the cephalic network developed out of the prolongation from the upper cervical ganglion the internal carotid nerve This cephalic network consists however as far as we know of efferent and not of afferent fibres (Danielopolu is practically a lone authority in maintaining that the cerebral sympathetic system contains afferent fibres (see Chapter XI)

To explain afferent effects in this network of efferent fibres the action of the vagus nerve is invoked The vagus it is contended brings afferent impulses to the superior sympathetic ganglion where motor cells are stimulated These cells in turn send impulses along the efferent brain fibres and produce effects such as constriction of facial and cerebral vessels (or coronary vessels in the thorax) disturbances in perspiration pain in the fifth cranial nerve and painful manifestations along the upper cervical plexus This conception as we shall see is based on clinical experience Patients in whom the cervical ganglionated chain was severed completely were able nevertheless to experience features of pain etc as described above Inasmuch as impulses could not pass through the interrupted cervical ganglionated chain it has been inferred that the vagal route acts as an accessory route and that a cephalic pathway for pain exists apart from the cerebrospinal axis For a fuller discussion of other relevant material see p 207

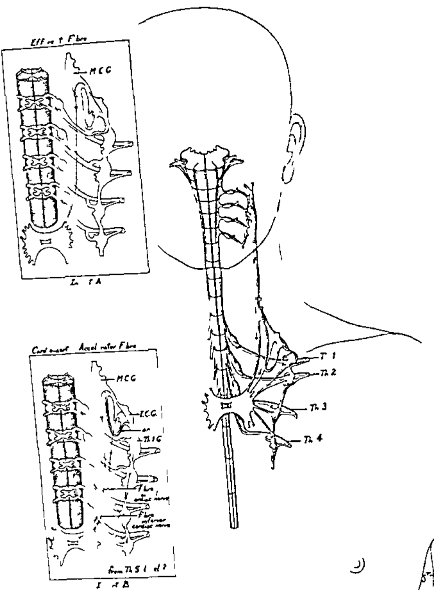


Fig 3a The Efferent Sympathetic Fibres

Fig 3 The Efferent Sympathetic Fibres Almost nothing definite is known of the intra spinal origin of the sympathetic efferent fibres cephalad to the upper thoracic levels At these levels and at corresponding lower levels these fibres emerge from the antero-lateral portion of the grey matter of the spinal cord and from each spinal cord level the fibres pass by way of white rami to corresponding ganglia in the sympathetic chain From this chain the efferent fibres form two groups (1) one group continues to peripheral structures (2) the other group to viscera in this case the heart The fibres of each group have a relay in the ganglia of the sympathetic chain or in ganglia within collateral plexuses or in the organs themselves Among the second group there are special fibres the accelerators with a regulatory action on the heart rate

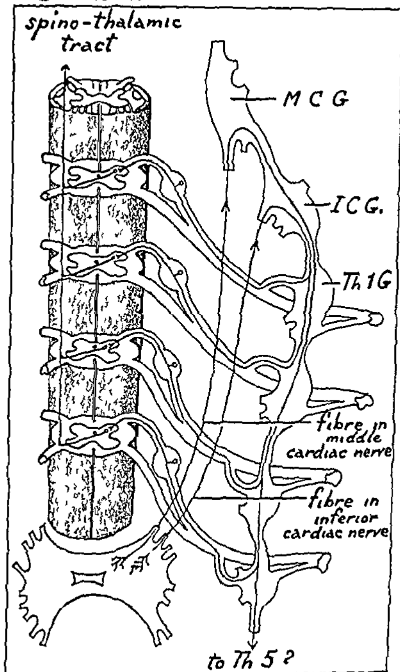


FIG. 34 Insert B Cardio aortic Afferent Fibres

b The ansa subclavia (Vieussens) The ansa or loop between the middle and lower cervical ganglia is a nerve strand that leaves the middle cervical sympathetic ganglion and runs downward It emerges from behind the common carotid artery and crosses the subclavian artery in front sending nerve twigs to it and to its vascular branches The loop turns around the subclavian artery lateral to the recurrent nerve receiving a few filaments from this nerve and ending in the inferior cervical (stellate) ganglion

In rare cases according to Danielopolu s description when the two components of the stellate ganglion have failed to fuse and are well separated as in the dog the ansa remains as an anterior and posterior division each acting as a connecting bridge between the two unfused components This loop contains afferent fibres from the heart and aorta Danielopolu believes afferent fibres run in the vertebral plexus and reach the loop The ansa also contains some cardio-accelerator (efferent) fibres

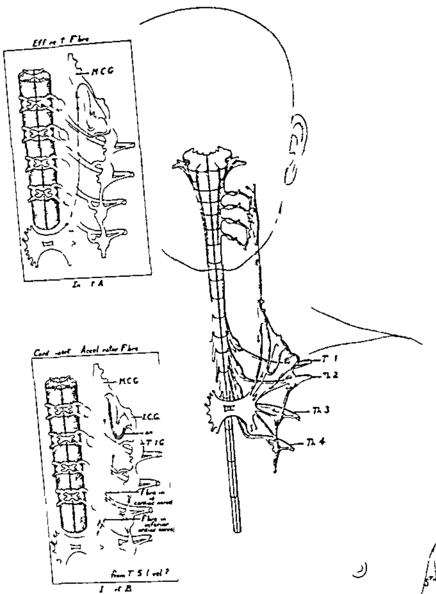


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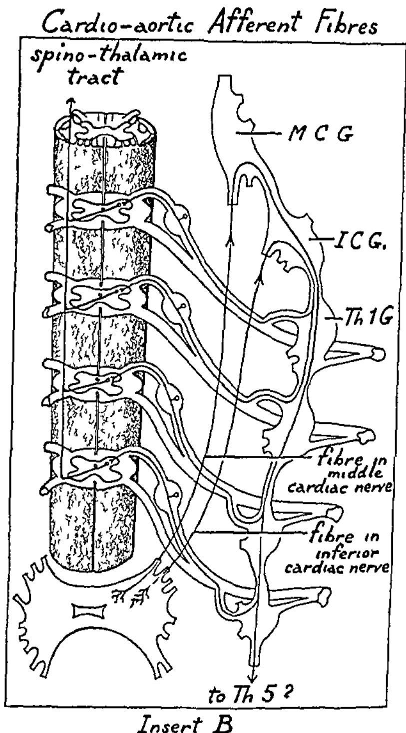


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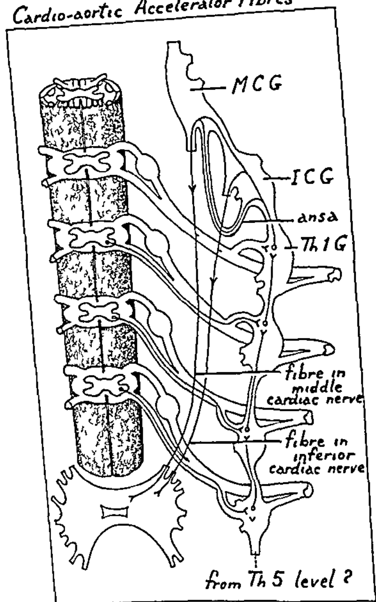
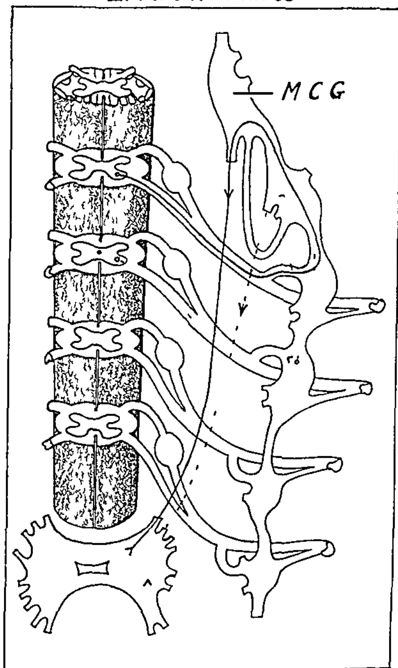


Fig 35 Insert B Cardio-aortic Fibres

Fig 35 Insert B The Efferent Cardio accelerator Fibres These fibres leave the spinal cord at Th 2 3 4 levels sometimes Th 1 and Th 5 and pass through ventral roots of the

Efferent Fibres



Insert A

Fig 35 Insert A Efferent Fibres

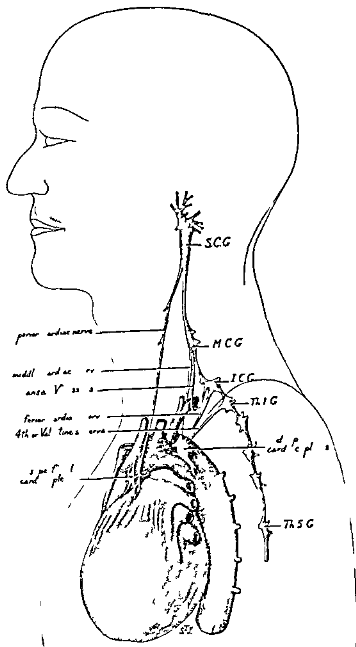


FIG 36 A Left Lateral View of the Sympathetic Cardiac Innervation The left sympathetic chain is clearly outlined also its three cardiac nerves one from each cervical ganglion to the cardiac plexuses the infrequent fourth Valentine's nerve is also included The left superficial cardiac plexus is placed more ventrally the left deep cardiac plexus lies behind it and at a slightly higher level. On the right side only a deep plexus exists The left superior cardiac nerve is connected with the superficial cardiac plexus the nerves of the other two sympathetic cervical ganglia with the deep plexus The three cardiac nerves communicate with one another the fourth the nerve of Valentine is not constant The specially differentiated loop the ansa Vieussens connects the middle and inferior (stellate) ganglia the loop curves under the subclavian artery

thoracic nerves and associated white rami to corresponding ganglia in the upper thoracic sympathetic chain Many fibres relay here those that emerge from the stellate or middle cervical sympathetic ganglion arrive at the cardiac plexuses by the inferior and middle cardiac nerves The presence of accelerator fibres in the superior cervical ganglion and superior cardiac nerve is disputed

Before reaching nerve endings in the heart sympathetic efferent fibres are broken by a relay in a ganglion of the upper thoracic or lower two cervical sympathetic ganglia as already indicated above or the relay takes place in a collateral ganglion i e in the cardiac plexuses or in an intracardiac ganglion In any event efferent fibres have a preganglionic and postganglionic component the former is myelinated and passes through white rami the latter is unmyelinated and in the case of non visceral fibres passes through grey rami

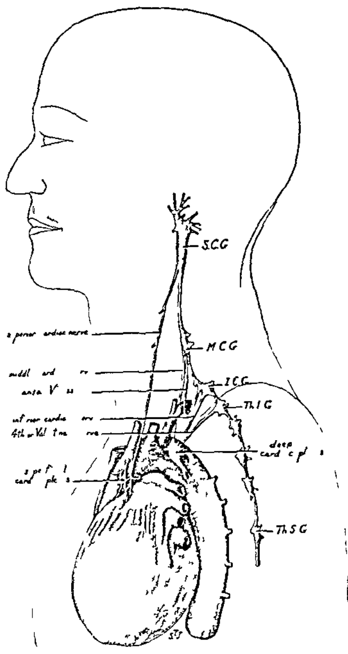


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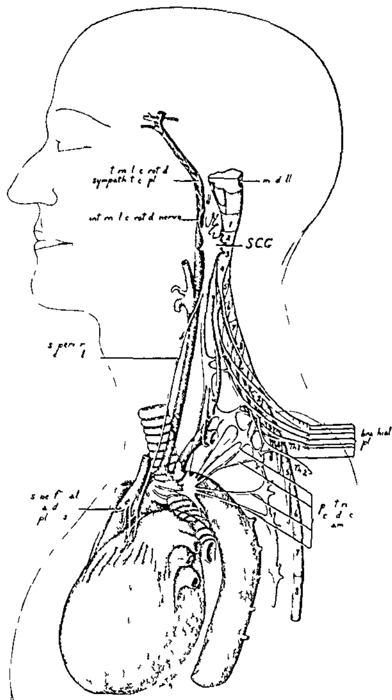


FIG 37 Left Lateral View (*continued*) This view illustrates the relations to the spinal cord to the brachial plexus and to the sympathetic distribution cephalad to the superior cervical ganglion The posterior cardiac sympathetic rami already depicted in a previous view (Fig 33 p 148) are readily seen in this drawing They connect the cardiac (and pulmonary) and aortic plexuses to the sympathetic ganglia of Th 1 2 3 4 Referred pain into the left arm is transmitted by means of a small portion of the brachial plexus This portion consists of the first and second thoracic nerves There are special but rarer circumstances when anginal pain enters the lower cervical nerves of the brachial plexus

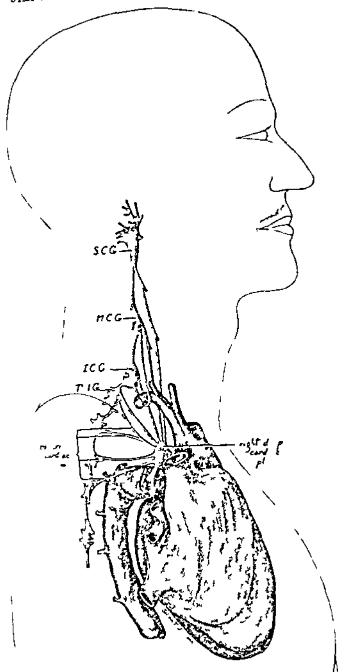


Fig 38 The Cardiac Sympathetic Innervation Viewed from the Right Side Only one cardiac plexus exists on this side a deep one into which all three cardiac sympathetic branches enter

Fig 39 The Cephalic Portion of the Sympathetic System The cephalic portion of the sympathetic system begins at the upper pole of the superior cervical ganglion as a distinct upward prolongation this prolongation evolved as an upward extension of the primitive sympathetic trunk develops an extensive network that follows the course of the cranial vascular supply (Fig 37 p 158) The network grows very diffuse (Fig 39 p 161) in it lie many tiny ganglia and plexuses and among these almost numberless ganglia and plexuses some are clearly defined practically constant in location and possess a special significance

Four macroscopic ganglia are prominent namely the ciliary or ophthalmic the sphenopalatine or Meckel s the otic and the submaxillary Of equal importance are the sympathetic components present in the nodosal petrosal geniculate and semilunar ganglia In many of the smaller plexuses minute nameless ganglia are imbedded

The upward extension of the superior cervical ganglion known as the internal carotid nerve forms two main plexuses The first is the internal carotid plexus and is developed by two branches that emerge from this internal carotid nerve A coarse plexus is formed that surrounds most but not all of the circumference of the internal carotid artery This internal carotid plexus sends shoots to the internal carotid artery and by fine filaments communicates with the semilunar (fifth nerve) ganglion and with the sixth nerve The plexus receives branches from the tympanic plexus through the inferior carotico tympanic nerve known also as the deep small petrosal nerve and from the spheno palatine ganglion via the deep petrosal nerve The internal carotid plexus with the same named artery pass through the carotid canal and reach the cavernous sinus At this point the plexus is called the cavernous plexus

The cavernous plexus sends communicating filaments to the third and fourth cranial nerves and to the ophthalmic division of the fifth nerve (According to some anatomists Toldt[20] also Spalteholz[25] the cavernous plexus is connected to the tympanic plexus by the small deep petrosal nerve) The cavernous sinus is connected to the ciliary ganglion by means of the long sensory root and also by a sympathetic motor root of the ciliary ganglion The plexus also gives off twigs to the carotid artery plexus and to the plexuse on the small arterial branches that enter the pituitary gland and the dura mater The cavernous plexus finally breaks up into delicate terminal filaments which anastomose freely forming fine plexuses on the terminal arterial twigs On these terminal divisions of the internal carotid artery nerves branches and plexuses take the name of the artery on which they lie the four largest forming the plexuses of the anterior and middle cerebral arteries

From the superior cervical sympathetic ganglion posterior branches reach the ninth the tenth and the eleventh cranial nerves and branches also go to the muscles and bones of the head and to the external carotid plexus with its arterial extensions and finally to the pharynx esophagus and larynx According to Danielopolu[5] François Franck demonstrated that the anastomoses between the superior cervical ganglion and the cranial nerves contain cardio aortic sensory fibres which influence the blood pressure through the bulbar vasomotor centers According to Danielopolu[5] also the anterior branch of the superior cervical ganglion together with the carotid plexus and cavernous plexus with its anastomosing branch for the Gasserian ganglion are of special importance in connection with the spread of anginal pain into the head

According to most authorities Danielopolu is an exception the cranial sympathetic supply contains efferent fibres only In order to explain sensory effects that are registered in the structures supplied by these efferent fibres it is held that afferent paths in the vagus (see footnote to the text for Fig 34 p 150) reach the upper cervical sympathetic ganglion stimulating its motor cells into action The effects of this are then distributed along the sympathetic cranial innervation We shall see however that afferent pathways in the vagus are able to go directly to the medulla (see Chapter VIII)

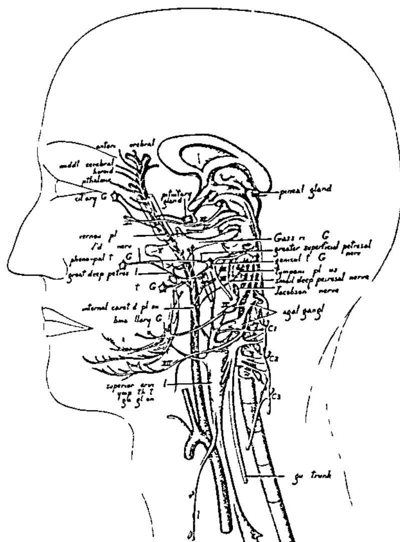


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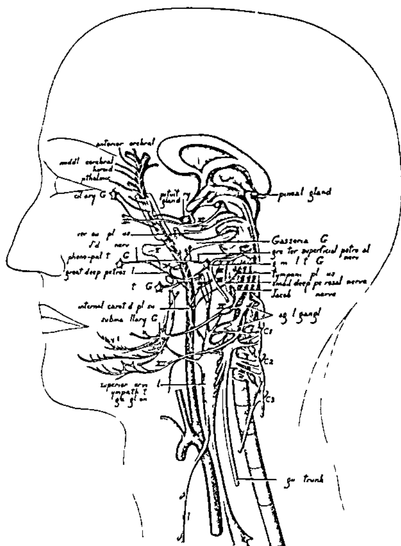


Fig 39 The Cephalic Portion of the Sympathetic System

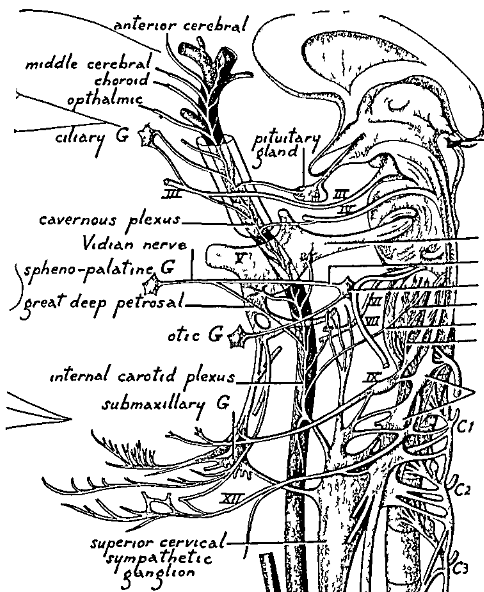


Fig 39A Enlargement of Part of Fig 39

Figs 40A and 40B The Cardiac Plexuses and Related Plexuses The location of these plexuses a deep one on each side and a superficial one on the left side only has already been mentioned They are made up of numberless fibers from the vagus and sympathetic cardiac nerves all three plexuses form one free anastomosing network. Tandler[27] claims the plexuses receive an inconstant nerve from the ansa hypoglossus.

The superficial cardiac plexus is located below the aortic arch immediately above the right pulmonary artery It is formed by the following structures (1) the left upper vagal cardiac branches from the vagus trunk (some texts Cunningham, etc mention the inferior group of these upper cardiac branches) (2) the left superior sympathetic cardiac nerve from the left superior cervical sympathetic ganglion (3) branches that communicate with the deep plexus on this

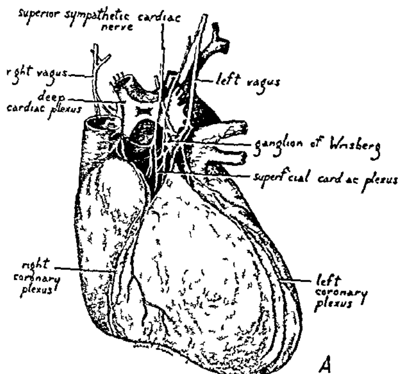


Fig 40A Front View of Cardiac Plexuses

left side (4 the cardiac ganglion (of Wrisberg) in this superficial plexus (5) and according to Tandler[27] the plexus occasionally receives fibres from the left inferior cardiac nerve and from the right cardiac inferior nerve and from rami from this nerve

From this superficial plexus branches go to the deep cardiac plexus to the right anterior coronary plexus and to the left anterior pulmonary plexus

The deep cardiac plexuses one on each side lie behind the aortic arch and anterior to the tracheal bifurcation Both plexuses communicate freely and may be looked upon as one network made up of (1) the right sympathetic cardiac superior middle and inferior nerves (2) the left sympathetic middle and inferior cardiac nerves (3) all the cervical and thoracic cardiac branches of the vagus excepting the left superior cardiac branch (4) the nerve of Valentine

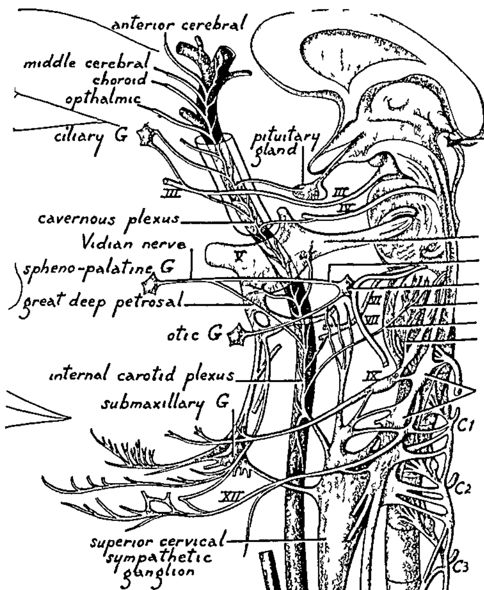


FIG 39A Enlargement of Part of Fig 39

FIGS 40A and 40B The Cardiac Plexuses and Related Plexuses The location of these plexuses a deep one on each side and a superficial one on the left side only has already been mentioned They are made up of numberless fibers from the vagus and sympathetic cardiac nerves all three plexuses form one free anastomosing network Tandler[17] claims the plexuses receive an inconstant nerve from the ansa hypoglossus

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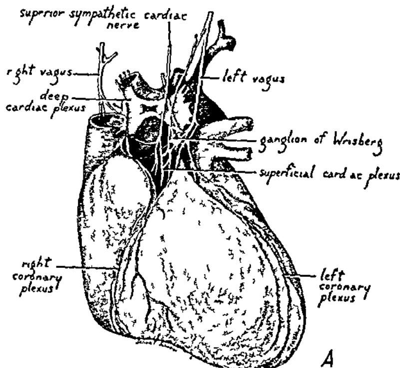


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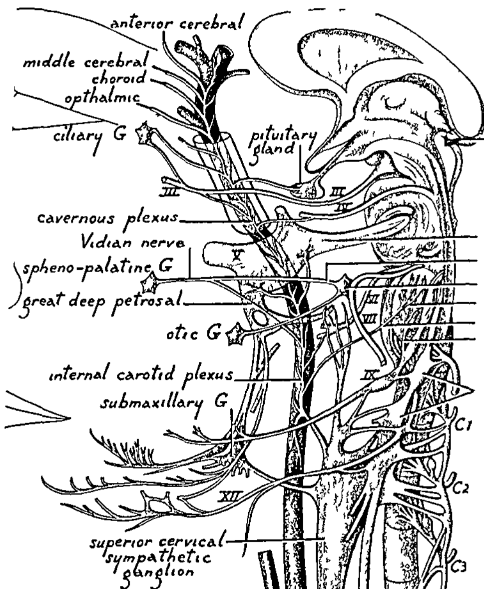


FIG 39A Enlargement of Part of Fig 39

In each layer these terminating nerve fibres have somewhat different arrangements In the epicardium they may or may not have a capsule Michailow[17] in the myocardium only the middle portion of the musculature receives plexal fibres the superficial musculature is innervated by the epicardial plexus close to it the inner musculature by an endocardial plexus A subendocardial layer exists also and consists of very fine fibers that penetrate the subendocardial layer Toldt[23] and extend to the ventricles auricles papillary muscles and papillary tendons

Fine ganglia probably exist in the heart substance Stöhr[26] In lower forms the calf for example they are plentiful Remak[19] first described them in man their presence is controversial. Authorities like Smirnov[2] Valedensky[4] described tiny ganglia in the wall of the ventricles down to the apex Jacques[8] Vignal[20] and Dogiel in the upper one third or one half of the ventricular wall only others limited to the sulcus area The ganglia in all instances appear to be placed superficially on the myocardium Wilson[21] is authority for finding them as multipolar ganglionated cells in the bundle of His and Tandler[27] in the posterior auricular wall terminal sulcus and interauricular septum There is no unanimity of opinion on the existence or location of motor nerve endings in the heart (Retzius[25]) it has been stated that only the myocardium contains them

Sensory nerve endings have been described in all three heart layers and Tandler stresses this pancardial arrangement The heart and large vessels have a rich sensory innervation Kolliker[22] Jegorow Dogiel[7] described rich supplies especially in the adventitia of the large vessels Manouelian[6] described sensory nerve endings in the aortic wall also Smirnow[2] who believed the spreading network he saw represented the origin of the depressor nerve The heart possesses an extensive supply of nerve endings according to Dogiel[7] Michaelow[17] Schmidt[21] Jacques Demoor[8] Woolward[22]

The pulmonary plexuses Branches from the 1st 2nd 3rd 4th thoracic ganglia and pulmonary branches of the vagus nerves unite to form a network behind the trachial bifurcation The network surrounds the trachea anteriorly and posteriorly and nerve fibres leave this network to accompany the pulmonary artery to the right and left hilus At the hilus anterior and posterior pulmonary plexuses are formed

The *esophageal* plexuses receive supplies from the cardiac plexuses

the fourth cardiac nerve arising from the 1st thoracic ganglionic component of the stellate ganglion, and (5) communicating twigs from the superficial plexus From these deep plexuses branches go to (1) the left and right antrum of the heart (2) to the left and right anterior pul monary plexuses (3) to the left and right coronary plexuses (4) and to the superficial cardiac plexus The deep cardiac plexuses as a whole separate into two good sized coronary plexu es, one to the right and the other to the left side

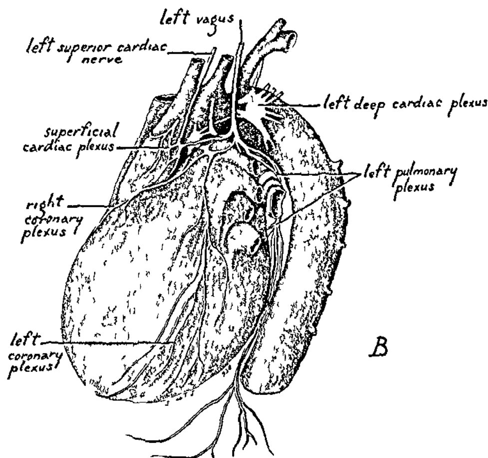


FIG 40B Lateral View of Cardiac Plexus

The right coronary plexus consists of fibres from the deep cardiac plexuses and from the superficial cardiac plexus and urrounds the aorta and the orifice of the right major coronary vessel This plexus follows chiefly the right ventricle and the right auricle

The left coronary plexus is formed mainly from the deep cardiac plexuse but the superficial cardiac plexus also sends fibres to it This coronary plexus runs downward behind the pulmonary artery to reach the origin of the left coronary artery and continues its ramifications so that one part of the plexus accompanies the course of the descending ramus of the coronary artery in this way reaching the anterior surface of the heart down to the apex the other portion of the plexus runs to the margo obtusus of the heart A very small part of this plexus reaches the posterior urface of the heart this surface is supplied mainly by the right coronary plexus

Spreading along perivascular connective tissues nerves from these plexuses form a fine net work and this in turn a delicate fibrillar network that ends in the epi myo endocardial layers

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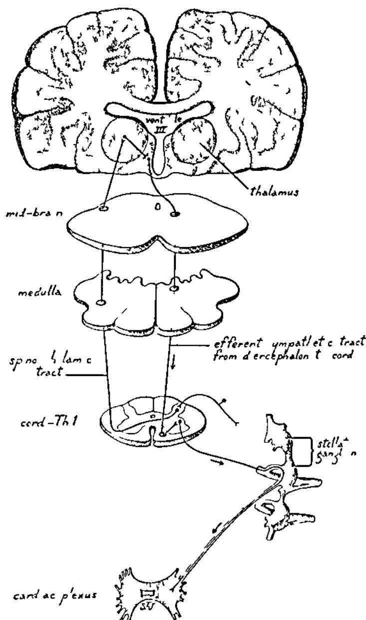


Fig 41 Fibres from the Hypothalamus to the Cardiac Plexuses This diagram is slightly modified after that of Beattie Brown and Long[1] It illustrates that fibre tracts pass down from the nuclei in the posterior part of the hypothalamus to the spinal cord The fibres emerge at the upper thoracic level reach the sympathetic stellate ganglion and thence the heart Experimental study on these tracts by these investigators is based on the earlier observations of Levy[15] who discovered that ventricular extrasystoles from chloroform anesthesia were abolished by extirpation of the stellate ganglion or by removal of the posterior hypothalamic nuclei Beattie Brown and Long not only confirmed this but they were able to trace spino hypothalamic tracts that underwent degeneration when nuclei in the posterior portion of the hypothalamus were experimentally damaged

BIBLIOGRAPHY

BEATTIE J BROW G K AND LONG C N H Proc Roy Soc London 1930 106 (ser B) 253-275

BRAEUCKER W Der Brustteil des vegetativen Nervensystems und seine klinischchirurgische Bedeutung Beitr z Klin d Tuberk 1927 66 1

CANNON W B LEWIS J T AND BRITTON S W A lasting preparation of the denervated heart, with evidence for accessory accelerator fibres from the thoracic sympathetic chain Amer J Physiol. 1929 77 326

CUNNINGHAM D J Textbook of anatomy 6th ed edit. by Brash J C and Jamieson E B Oxford University Press 1931

DANIELOPOLU D L angine de poitrine et l angine abdominale Paris, Masson et Cie 1927

DEMOOR ET HEYMANNS Etude d l innervation du coeur des vertebres à l aide de la methode de Golgi Arch d Biol 1894 13

DOGIEL, A S Die sensiblen Nervenendigungen im Herzen und in den Blutgefasse der Saugetiere Arch f mikroskop Anat. 1898 52 44 Zur Frage über den feineren Bau der Herzganglion der Menschen und der Saugetiere Arch. f mikroskop Anat 1899 53 237

FRANCK F Quoted by Danielopolu D L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

JACQUES P Récherches sur les nerfs du coeur chez la grenouille et les mammifères. J d L Anat et d la Physiol 1894 30 63

JEGOROW I Zur Lehre von der Innervation der Blutgefasse Du Bois Arch Supplementary volume 1892 69

JONESCO D AND ENACHESCO M Comp Rend Soc d Biol 1927 97 977 an 1980

VON KOLLIKER A Untersuchungen über di letzten Endigungen der Nerven *Zeitschr f* wiss Zool 1863 12 149

KUNTZ A Distribution of sympathetic rami to the brachial plexus Arch Surg 1927 15 871

KUNTZ A AND MOREHOUSE A Arch Surg 1930 20 607

LEVY A G The exciting causes of ventricular fibrillation in animals under chloroform anesthesia Heart 1913 4 319

The genesis of ventricular extrasystoles under chloroform with special reference to consecutive fibrillation Heart 1914 5 299

Further *remarks on* ventricular extrasystoles and fibrillation under chloroform Heart 1919 7 105

MAXIMOW? CELLAN Recherches sur le plexus cardiaque et sur l innervation de l aorte Ann. d l Inst Pasteur 1912 28

MICHAILOW S Ein *neuer Typus* eines eingekapselten sensiblen Nervenendapparates Anat Anz 1907 31 81

Das intrakardiale Nervensystem des Frosches und die Methode von Ramon y Cajal Internat Monatsschr f Anat u Physiol 1908 25 351

Die Nerven des Endokardiums Anat Anz 1908 3 8

Zur Frage uber den feineren Bau des intrakardialen Nervensystems der Säugetiere Internat Monatschr f Anat u Physiol 1908 25 44

Innervation des Herzens im Lichte der neuesten Forschungen Zeitschr f wiss. Zool 1912 99 535

MIXTER W J AND WHITE J C Pain pathways in the sympathetic nervous system Clinical evidence Arch Neurol and Psychiat 1931 25 986

REMAK R Neurologische Erlauterungen Müllers Arch 1844 5 463

RETZIUS G Zur Kenntnis der motorischen Nervenendigungen Biol Unters 1892 3 41

SCHMIDT A Sur la question de l innervation du coeur de mammifères Arch. russ. de path et de Méd Clin et de Bactér 1897

[22] VON SCHUHMACHER S Zur Frage der Herzinnervation bei den Saugetieren Anat Anz 1902 *21* 1 430
Die Herznerven der Saugetiere und der Menschen Sitzungsber d Akad Wien Mathem naturw Klin 1903 Abt 3
Beitrage zur Kenntnis des Baues und der Funktion der Lamellenkörperchen Arch f mikroskop Anat 1911 *77* 157
[23] SINGER R AND SPIEGEL F A Der Weg des Herz und Aortenschmerzes über die Hinterwurzeln zum Zentral Nervensystem Zeitschr f d ges exp Med 1927 *55* 607
[24] SMIRNOW A Über die sensiblen Nervenendigungen im Herzen bei Amphibien und Säugetiere Anat Anz, 1895 *10* 737
Zur Frage von der Endigung der motorischen Nerven in den Herzmuskeln der Wirbeltiere Anat Anz 1900 *18* 105
[25] SPALTEHOLZ W *Handatlas of human anatomy Translated 6th ed Philadelphia* and London J B Lippincott & Co vol 3
[26] STOHR P JR Mikroskopische Anatomie des vegetativen Nervensystem Berlin J Springer 1928
[27] *TANDLER J Anatomie des Herzens In Bardelebens Handb d Anat 1913*
[28] TOLDT C Anatomische Atlas 16 Aufl Berlin u Wien Urban u Schwarzenberg 1934 vol 3
[29] VALENDENSKY A Zur Frage uber die Nervenknoten im Herzventrikel einiger Saugetiere *Anat Hefte* 1905 *27* 287
Einige Ergänzungen zur Frage nach der Gegenwart und der Verteilung der Herzganglion in den Herzkammern einiger Saugetiere und des Menschen Anat Anz 1910 *37* 365
[30] VIGNAL W Recherches sur l appareil ganglionnaire du coeur des vertébrés Arch d Phys siol 1881 vol 3 (ser 2)
[31] WILSON J G The nerves of the atrio ventricular bundle Proc Roy Soc London vol 81 (ser B)
[32] WOOLLARD H H Innervation of the heart J Anat 1926 *60* 345

Other references and hand atlases consulted in the preparation of this chapter are listed below

BOURGERY J M AND JACOB N H Traité complet de l anatomie de l homme comprenant *le médecine opératoire avec planches d après nature Paris C A Delaunay* 1831 and 1854
BRAUS H Anatomie des Menschen Centrales Nervensystem von Curt Elze Berlin J Springer 1925
DEJERINE J J Semiologie des affections du systeme nerveux Paris Masson et Cie 1924
GRAY H Text book of anatomy 1935
MAXIMOW A A A textbook of histology Completed and edited by Bloom W Philadelphia Wm Saunders Co 1930
MORRIS H Human anatomy 1933
PENSA A AND FAVARO G Trattato di anatomia sistemica Torino Unione tip edit Torinese 1933
PIERSOL G A Human anatomy 9th ed 1930
PITRES A AND TESTUT L Les nerfs en schémas anatomie et physiopathologie Paris G Doin et Cie 1925
SABOTTA J Atlas der deskriptiven Anatomie des Menschen J F Lehmann 9 aufl München 1937
TESTUT L Traité d anatomie humaine 8th ed Revue par Latarjet A Paris G Doin et Cie 1928
WALDREN J AND GREEN R M Handbook of anatomy Harvard University Press Cambridge Mass 1934

CHAPTER VIII

The Vagal Supply to the Heart and Aorta

THE VAGUS nerve consists of a large and extensive system of which the cardio-aortic innervation is but a smaller part To understand the anatomic and physiologic relations of the cardioaortic innervation other portions of the vagus system are included At the onset the question is relevant is the vagus truly an afferent conductor of cardio-aortic pain? That it transmits pain from the musculature for example of the bronchi the intestines is not disputed but a similar activity with respect to the cardiovascular structures is not as definite In its primitive form the vagus is a cardio-gastric nerve later in higher animal forms it assumes a pulmonary function but it retains always its primary character as a supervisor and regulator of the heart and aorta of the gastro-intestinal tract and of the lungs For the transmission of cardio-aortic pain the sympathetic nerves are adequate in every way and many experimental and clinical observations are on hand to demonstrate that severing of sympathetic routes will abolish pain Similar conclusive data on the cardio-aortic vagal innervation does not exist as far as we know

A description of the vagal supply to the heart and aorta however cannot be omitted first because vagal manifestations of angina pectoris are part of the mass action of the autonomic system second because dramatic *constrictive features* in the throat in the epigastrium and in the chest itself are induced by motor nerves which belong in this system third the vagus regulates the heart rate influences the amplitude of heart muscle contraction and through the aorta controls changes in blood pressure lastly the vagus in some portions and under some circumstances acts in a way to permit the interpretation that it may be an accessory conductor of pain

The vagal cardio-aortic innervation possesses a large number of fibers that enter the cardio-aortic plexuses connecting with many other plexuses in the thorax (Fig 46 47 48 also Chapter IX) *In all these* plexuses vagal fibers mingle freely but effect no anosculations with similar plexal fibers of the sympathetics The tracts for the heart and aorta from the vagus spring from the trunk ganglia and in the cervical region from the trunk and the right recurrent laryngeal nerve in the thorax from the trunk and the left recurrent laryngeal nerve From the cardiac and aortic plexuses afferent fibers are described as running upward to the trunk ganglia and thence into the medulla where the fibers reach vagal nuclear structures and where they may intersect cranial nerve fibers notably those in the sensory component of the fifth nerve Afferent

fibers run between the trunk ganglia and the superior cervical sympathetic ganglion In these ganglia lie nuclei of (motor) efferent fibers that supply cranial structures

A special nerve strand, the depressor nerve is considered by some authorities as a separate distinct afferent pathway A description of this nerve will be found in Chapter IX

The vagus has many anatomical connections with other nerve structures (Fig 45, p 176) In the chest and neck, its cardiac branches communicate freely with the branches of all the cervical sympathetic ganglia It sends connections into the ansa Vieussens and shares richly in the formation of many plexuses in the chest and neck In the cervical region it anastomoses with the 1st and 2nd cervical nerves bringing pain into the structures supplied by these nerves Its cephalad connections into the superior cervical ganglion and its entry and *termination into the medulla have already been mentioned* Vagal fibers have also been discovered in the sympathetic innervation, for example in the superior sympathetic cardiac nerve Such fibers have been traced to the vagal trunk ganglia and are an example of the presence of fibers of one autonomic division within the other division This interplacement is not of great moment according to our present understanding, since the fibers of each division retain their inherent physiological character cholinergic or adrenergic The anastomoses between the vagus and various portions of the sympathetic system and the profuse mingling of end fibers of both systems in many plexuses is probably of anatomic interest only and without any implication that impulses from one autonomic division actually pass into the other autonomic division

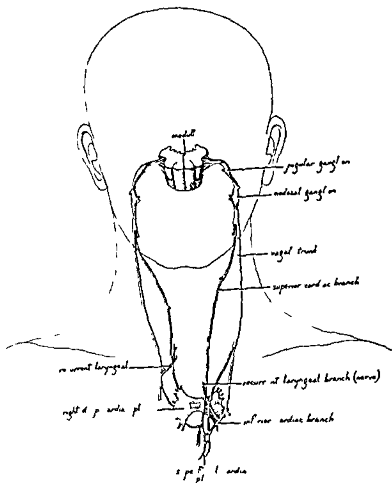


FIG 42 The Vagus Nerve from the Brain to the Cardiac Plexuses

FIG 42 The Vagus Nerve from the Brain to the Cardiac Plexu es The heart and related structures recei e a vagal as well as sympathetic innervation With exceptions to be noted later the vagus nerve has a general symmetrical distribution

In the medulla the vagus has two effector nuclei and one receptor tract The nuclei consist f (1) the d rsal motor nucleus wh ch is purely sympathetic in its action and (2) the nucleus ambiguus which is somatic (motor) in function and is therefore un ler voluntary control

Fibres from the second nucleus (ambiguus) go to other cranial nerves and in connection with angina pectoris, are of special interest by virtue of their innervation of laryngeal muscles. The receptor station the nucleus of the tractus solitarius is a longitudinal column of cells with which dendrites of the tractus solitarius make connections The visceral afferent fibres that run in the vagus system have their cell bodies in the trunk ganglia chiefly in the nodosal The central extensions of these fibres proceed to the nucleus of the tractus solitarius and form synaptic connections with it

From the upper ganglion of the trunk the jugular ganglion smaller and higher than the nodosal two branches emerge (*1*) a meningeal to the dura mater in the posterior fossa of the base of the skull and (*2*) an auricular branch the so called Arnold s nerve This latter communicates with (*a*) the tympanic branch of the glosso pharyngeal nerve (*IX*) and with the facial nerve within the aqueduct of Fallopius The auricular nerve supplies the back of the pinna of the ear the bony part of the external auditory canal and the outer surface of the lower portion of the tympanic membrane The nerve communicates superficially with the posterior auricular nerve The jugular ganglion anastomoses with (*1*) the superior cervical sympathetic ganglion (*2*) the spinal accessory nerve and (*3*) the petrous ganglion of the glosso pharyngeal nerve (not constant)

The nodosal ganglion is larger lower and has the following branches (*1*) A pharyngeal nerve which forms the pharyngeal plexus with the pharyngeal branch of the glosso pharyngeal nerve and with the branch from the superior cervical sympathetic ganglion This plexus spreads *to the muscles of the pharynx and soft palate excepting the stylo pharyngeus and tensor palati* muscles (*2*) A superior laryngeal nerve which divides into two unequal divisions (*a*) a large internal laryngeal nerve and (*b*) a small external laryngeal nerve The former is distributed to the mucous membranes of the larynx reaches the epiglottis and the base of the tongue and communicates with the inferior laryngeal nerve The small external laryngeal nerve supplies the inferior constrictor muscles of the pharynx and ends in the crico thyroid The nodosal ganglion communicates with (*1*) the superior cervical ganglion (*2*) the hypoglossal nerve (*3*) the loop that connects the first and second cervical nerves and (*4*) the accessory portion of the spinal accessory nerve

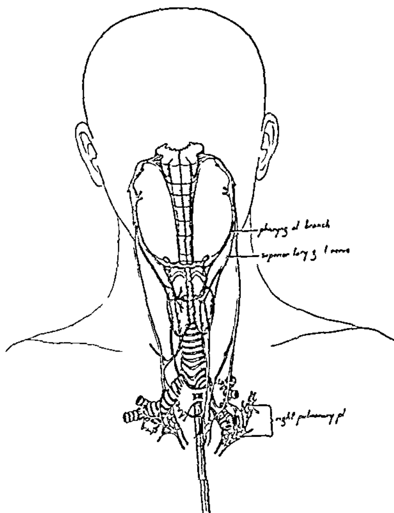


FIG 43 The Vagus Nerve (continued)

FIG 43 The Vagus (continued) *The cervical branches* These arise in the neck and consist of (*1*) cardiac branches and (*2*) the right recurrent laryngeal nerve

(*1*) The cardiac branches come off the trunk There are upper and lower groups or divisions of these fibres On the right side both sets upper and lower descend into the thorax behind the subclavian artery and then proceed along the side of the trachea to enter the deep cardiac plexus On the left side both groups separate as they enter the thorax The superior division (or nerve) descends along the trachea and goes to the left deep cardiac plexus the inferior

division (or nerve) runs alongside the vagus trunk to the aortic arch and thence to the superficial cardiac plexus

(2) The right recurrent laryngeal *(inferior laryngeal) nerve springs from the trunk of the* vagus at the root of the neck, as the trunk crosses the first part of the subclavian artery This recurrent nerve swings around this artery and then travels obliquely upward inward and behind this vessel as well as the common carotid the inferior thyroid arteries and the thyroid gland The innervation of the laryngeal muscles represents the termination of this nerve The following branches leave it in its course

(a) Branches to the cardiac plexus These fibres emerge as the nerve proper curves around the subclavian artery they descend along the trachea and as thoracic branches end in the deep cardiac plexus *(b)* The other branches of the right recurrent nerve have at most an indirect relationship to the cardio aortic innervation They are as follows communicating fibres to the inferior cervical sympathetic ganglion these emerge from the nerve behind the subclavian artery muscular branches to the trachea esophagus and the inferior constrictor muscle to the pharynx terminal fibres that supply all the laryngeal muscles excepting the *crico-thyroid and fibres that communicate with the internal laryngeal nerve*

Thoracic branches The thoracic cardiac nerves consist of the left recurrent laryngeal nerve and its branches to the heart and thoracic cardiac branches

The left recurrent laryngeal nerve leaves the vagus trunk as the latter crosses the aortic arch The recurrent nerve winds around the aorta external to the ligamentum arteriosum and lying between the trachea and esophagus it ascends the superior mediastinal space to the neck The course and relation of both recurrent laryngeal nerves is the same in the neck The branches of the left nerve are larger and having a shorter distance to travel to join the left deep cardiac plexuses they are accordingly much shorter Thoracic branches leave the vagus trunk in the superior mediastinal compartment and descend along the trachea to the right deep cardiac plexus

On the left side the thoracic branches consist of those that leave the loop of the left recurrent laryngeal nerve

In addition to these left recurrent fibres there are other thoracic vagal fibres for the heart These spring directly from the vagus trunk in the superior mediastinal compartment and descend along the trachea to the right deep cardiac plexus The thoracic fibres on the left side are the continuation of the cervical branches that emerge from the loop of the left recurrent laryngeal nerve

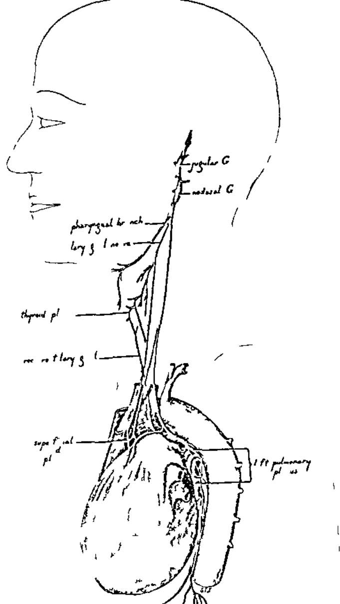


FIG 44 A Lateral View of the Left Vagus Nerve The upper divisions of cervical vagal branches converge upon the pharynx larynx and thyroid regions A lower division descends to the superficial cardiac plexus on this side as already stated The recurrent laryngeal (inferior laryngeal) nerve on this side winds around the aortic arch and then ascends alongside the deeper aspect of the trachea finally communicating with branches of internal laryngeal nerve It has an anastomosis with the branch of the inferior cervical sympathetic ganglion The cardiac fibres that leave the loop of this recurrent nerve form a thicker larger and shorter bundle compared with the right side The other branches of this nerve have already been described.

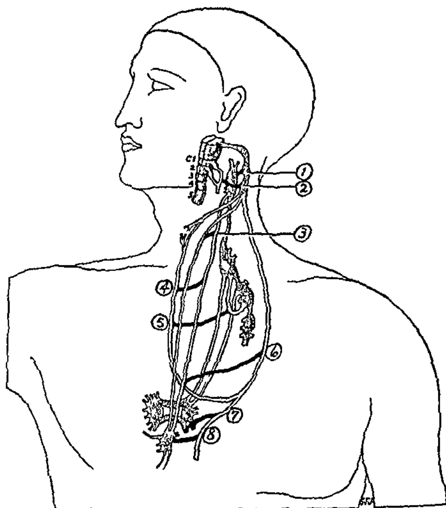
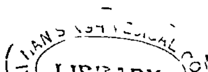


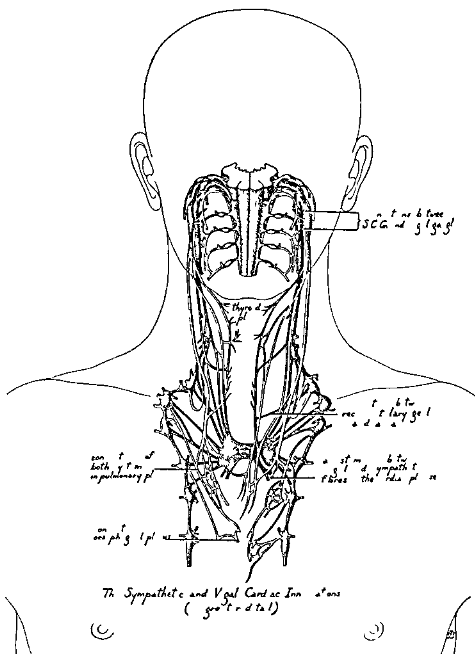
Fig 45 Connections between the Vagal and Sympathetic Systems in Relation to Anginal Pain *1* Connections between the superior sympathetic cervical and the vagal ganglia *2* Vagal connections to C 1 and 2 *3 6* Connections between the superior branches of both systems Similar communications connect the middle and inferior branches *4* Anastomoses between the recurrent laryngeal nerve and the superior sympathetic branch *5* Connections between the recurrent laryngeal nerve and the ansa *7* Anastomoses between the vagal and sympathetic fibres at the cardiac plexus *8* Vagal connections into the superficial cardiac plexus

Note particularly these relationships and how they lend support but no proof that stimuli from one system might "overflow" into the other system especially at the level of the superior cervical sympathetic ganglion and of the trunk ganglia of the vagus This would make it possible for afferent vagal impulses to reach the brain structures through the superior sympathetic cervical ganglion even if the cervical ganglionated chain below this level were interrupted

Th Sympath t and V g l Card ac Inn rvat ons

FIG 46





Th Sympathet c and V gal Card ac Inn at ons
(gre t r d ta l)

FIG 47

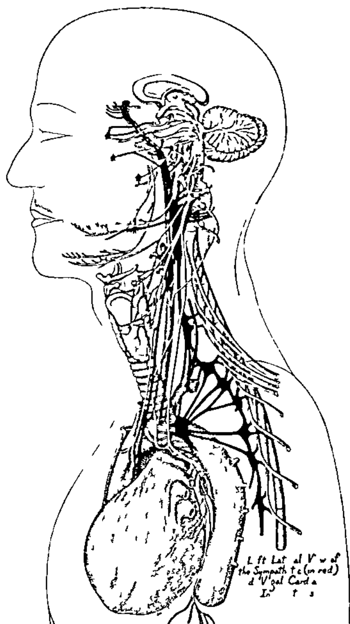


FIG 48

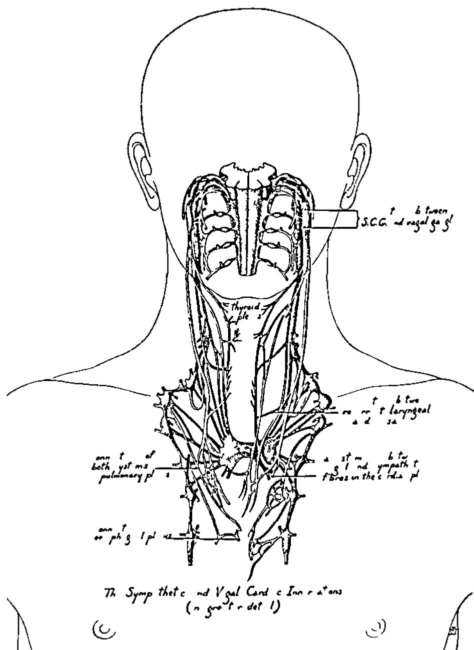


FIG 47

cation has an additional and speculative interest The ansa loop is brought into relation with the sympathetic vertebral plexus and if it be accepted as some maintain that the plexus contains afferent cardio-aortic fibers this relationship would point to another afferent cardio-aortic pathway with which the recurrent nerve of the vagus would have anatomic contact The third anastomosis between the trunk ganglia of the vagus and the superior cervical sympathetic ganglion is well defined anatomically but has failed to reveal any afferent cardiac fibers for the transmission of impulses except those alluded to in Chapter XI traversing the superior cervical ganglion but destined for the vagal ganglia Hembecker *

In addition there are a number of other anatomic connections between vagal and sympathetic nerves which are inconstant and variable Murray[17] found that the superior sympathetic cardiac nerve sometimes entered the vagal trunk Braeucker[3] described connections between the superior sympathetic ganglion and the superior laryngeal nerve and Tandler[22] between the sympathetic cardiac branches and the superior laryngeal nerve The superior cardiac nerve has been observed to have one vagal root a superior laryngeal derivation and the other sympathetic Danielopolu[8] quoted Brock[4] as having seen this nerve arise from the inferior laryngeal and glosso-pharyngeal nerves Into the pharyngeal and laryngeal plexuses go branches of the vagus nerve and branches from the superior cervical sympathetic ganglion a possible connection is implied here Hirschfeld[16] found anastomoses from the vertebral nerve to the middle sympathetic ganglion and to the cervical sympathetic trunk (this unusual anastomosis is entirely sympathetic) From the inferior cervical sympathetic ganglion occasionally there are branches to the recurrent laryngeal nerve Fibers of both systems sometimes lie in the same tract or bundle Testut[23] and the probability that vagal fibers (cholinergic) run in the sympathetic cord served Tigerstedt[4] as the basis for his explanation of the odd and rare observation by Wagner[27] and Bezold[2] that cardiac inhibition followed stimulation of the cervical sympathetic cord *

All these anastomoses unusual and usual are decidedly more numerous in man than in animals the variability is also greater in man The rich intercommunicating arrangement of all the connections described above seems to suggest two possibilities one a better and more readily integrated physiologic control over aortic and cardiac functions and two a readily accessible means for short-circuiting centripetal impulses from one system into another The second possibility might be especially useful in emergencies that result from interruption or permanent damage to important routes in the cardiac innerva

* This assumption of Tigerstedt and similar observations by others anticipated the discovery in very recent years that cholinergic fibres usually in the vagal system occur also in the sympathetic innervation and that adrenergic fibres usually in the sympathetic system run within the vagal nerves The mass action of the autonomic system see (Chapter IX) expresses itself as cholinergic or adrenergic reactions regardless of the location of these fibres

CHAPTER IX

The Anastomoses between the Sympathetic and Vagal Systems

THE SYMPATHETIC and vagal nerves *to the heart have uncountable num* bers of fine twigs and fibers that form plexuses (Fig 47, p 178) These plexuses of which the cardiac are an example consist of masses of closely inter woven fibers but with no synaptic arrangements and with no interfusion or anastomoses *of nerve fibrils from one system into another No physiologic proof* exists that this mingling is more than an anatomic relationship We have, therefore no basis for believing that impulses in one system pass to the other in the vast network of the cardiac and other plexuses Both systems in general are linked to many similar *networks in the thorax neck and head* and it is more than probable that by means of the cardiac innervation of each system reflex activity is registered in almost any of the non cardiac plexuses (Fig 47, p 178) On this basis it is possible to assume that cardio aortic afferent im pulses are brought into relation with esophageal laryngeal, pharyngeal, thy roid and pulmonary plexuses and with those in the brain also Some of the results that follow from this are described in Chapter XI among them the pre vention of anginal pain by thyroid ablation and unavoidable disruption of the thyroid plexus

The anatomic independence* of both cardiac innervations is clearly pre served yet there are a number of places where both systems anastomose Three, at least deserve special mention (1) the rather extensive web of communi cating fibers between the cervical sympathetic and vagal cardiac nerves (these nerves descend in the neck and chest and their anastomoses are in the neck and chest Figs 31 45 p 145 and p 176) (2) the anastomoses between the re current laryngeal nerve and the ansa loop (Fig 34 Insert A Fig 45 p 176) (3) and the connections between the superior cervical sympathetic ganglion and the jugular and nodosal ganglion of the vagus (Figs 45 47 p 176 and p 178) We cannot say whether these anastomoses in general are more pronounced on the left side although it is recognized that the cardiac innervation in toto is fuller and more extensive on this side This has been attributed to the greater development size and work of the left heart

These anastomoses are richer in man than in animals and more variable The three communicating arrangements cited above however are fairly con stant The first is a rather coarse and extensive interbranching web or network and unlike other networks is not primarily perivascular The second communi

* For a discussion of the unitary physiological action of both divisions see Chapter IV

have produced a sharp decline in blood pressure by sectioning the depressor nerve but already in 1868 Aubert and Koever[1] had obtained a similar result by stimulating the caudal end of the cervical sympathetic chain François Franck[8] obtained the same effect attributing it to a sudden dilatation of peripheral as well as splanchnic blood vessels These physiologic responses suggested that the action of the depressor nerve may be sympathetic in nature and mediated perhaps through intimate anatomic connections with the sympathetic innervation Although similar anatomic connections in man have not yet been established there is no question of the occurrence of similar human cardiovascular manifestations identical with those attributable to the action of the depressor nerve in lower forms

Our interest in the depressor nerve in man is twofold first as a pathway for the transmission of impulses that regulate the cardiovasular phenomena just described These impulses are set off primarily in the proximal portion of the aorta (see Chapter XI) According to Hering[10] Koch[11] and Heymans[11] the carotid sinus at the bifurcation of the common carotid artery functions in a similar manner Second the depressor nerve has been the object of surgical attack for the relief of anginal pain (see Chapter XXII)

BIBLIOGRAPHY

AUBERT H AND ROEVER G Quoted by Danielopolu D in L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

[4] BERNHARDT E Anat u phys Untersuchungen uber den Nervus Depressor bei der Katze Med Disc Dorpat 1868

[5] BEZOLD A v In Tigerstedt R Physiologie des Kreislaufes Berlin de Gruyter 1921 23

BRAEUCKER W Beitr z Klin d Tuberk 1927 66 1

BROCK Quoted by Danielopolu D in L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

[6] DE CYON E AND LUDWIG C Berichte der K Sachs Ges d Wiss 1866 Jour d An et de Phys 1867 4 472 Gesammelte Physiologische Arbeiten Berlin 1888

DANIELOPOLU D L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

FINKELSTEIN A Der Nervus Depressor beim Menschen Kaninchen Hunde bei der Katze und dem Pferd Arch f Anat Abt 1880 245

[8] FRANCK F Signification physiologique de la resection du sympathetique dans la maladie l epilepsie l idiotie et le glaucoma Bull de l Acad de Med 1899 41 565

HEINBECKER P Anatomic and physiologic criteria for surgical relief of cardiac pain J Thoracic Surg 1932–33 2 517

HERING H E Die Karotissinusreflexe auf Herz und Gefasse Dresden u Leipzig 1927 Pfluger's Arch 1924 206 721

[11] HEYMANS C BOUCKAERT J J AND REGNIERS P Le sinus carotidien C D in et Cie Paris 1933

HIRSCHFELD F G Angina pectoris saturnin Inaug Disc Berlin 1926 Zeitschr f klin Med 104

HOFER G Die chirurgische Behandlung der Angina Pectoris Wien klin Wchnschr 1924 37 Suppl (July 10) 1924 1

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tion But these possibilities have not as yet received physiologic or experimental confirmation

We include in this chapter on anastomoses between both divisions of the cardiac innervation a consideration of the so called depressor nerve because it is not known whether this structure functions as a vagal or sympathetic pathway or by its anatomic connections brings both types of fibers into action In all likelihood a pathway corresponding to that of the depressor nerve in lower forms exists also in man In animals, at least, the nerve runs as a separate and independent vagal strand between the aorta and the upper part of the vagus trunk or the ganglia of the trunk Only a few anatomists have claimed that the depressor nerve in man is a well defined structure Viti[6] maintained it existed as an isolated nerve resembling the condition in the rabbit Koster and Tschermack[1] believed the nerve ran from the aorta to the upper part of the vagus, (they called it the aortic nerve), but Vanesco[25] as well as Danielopolu, was able to follow the nerve to the posterior cardiac plexus and even to the heart itself Vanesco claimed the depressor nerve, or, at least a structure that resembled it, often replaced an absent left superior vagal cardiac nerve and he agreed with Hofer[13] that this sinistral frequency was greater and that the nerve was seldom present on both sides in the same subject Other authorities Scarpa [0] Sappey,[19] Bernhardt[2] found the depressor arising from the laryngeal nerves of the vagus and Finkelstein[7] Schwalbe[1] Hofer reported that the depressor had its origin in or else replaced, the cardiac branches of the vagus Kreidemann[16] stated the depressor nerve was made up of variable nerve filaments The lack of agreement on the anatomy of the nerve has made it a subject of considerable study and still more controversy, but the consensus at present is that in man the nerve does not exist as a well defined macroscopic structure

In animals however, there are apparently a number of authentic identifications of the nerve The original publication of Cyon and Ludwig[5] is authoritative and describes a separate strand in the rabbit the excitation of which caused a prompt fall in blood pressure In this animal too anatomic deviations were encountered the depressor receiving connections from the sympathetic system but its predominant character as a vagal nerve was not questioned Danielopolu in the dog discovered combined vagal and sympathetic fibers in the depressor nerve and he ascribed the slowing of the heart to the part played by vagal fibers and the change in blood pressure to that of the sympathetic fibers He published experimental proof of the sympathetic pressor action of the nerve

The physiology of the nerve has received extensive study in animals chiefly in rabbits and dogs Distal stimulation of the cut nerve produces a prompt fall in the general blood pressure and a slowing of the heart rate This effect was described by Cyon and Ludwig in their original publication repeated by Koster and Tschermack, and confirmed later by Osborne[15] Tigerstedt is reputed to

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BIBLIOGRAPHY

AUBERT H AND ROEVER G Quoted by Danielopolu D in L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

[2] BERNHARDT E Anat u phys Untersuchungen über den Nervus Depressor bei der Katze Med Disc Dorpat 1868

[11] BEZOLD A v In Tigerstedt R Physiologie des Kreislaufes Berlin de Gruyter 1921 23

BRAEUCKER W Beitr z Klin d Tuberk 1927 66 1

BROCK Quoted by Daniélopolu D in L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

[5] DE CYON E AND LUDWIG C Berichte der K Sachs Ges d Wiss 1866 Jour d An et de Phys 1867 4 477 Gesammelte physiologische Arbeiten Berlin 1888

DANIÉLOPOLU D L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

FINKELSTEIN A Der Nervus Depressor beim Menschen Kaninchen Hunde bei der Katze und dem Pferd Arch f Anat Abt 1880 245

[8] FRANCK F Signification physiologique de la resection du sympathetique dans la maladie l epilepsie l idiotie et le glaucoma Bull de l Acad de Med 1899 41 565

HEINBECKER P Anatomic and physiologic criteria for surgical relief of cardiac pain J Thoracic Surg 1932 33 2 517

HERING H E Die Karotissinusreflexe auf Herz und Gefasse Dresden u Leipzig 1927 Pfluger's Arch 1924 206 721

HEYMANS C BOUCKAERT J J AND REGNIERS P Le sinus carotidien G Doin et Cie Paris 1933

HIRSCHFELD E G Angina pectoris saturnin Inaug Disc Berlin 1926 Zeitschr f Klin Med 104

[3] HOFER G Die chirurgische Behandlung der Angina Pectoris Wien klin Wchnschr 1924 3 Suppl (July 10) 1924 1

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BIBLIOGRAPHY

AUBERT H AND ROEVER G Quoted by Danielopolu D in L'angine de poitrine et l'angine abdominale Paris Masson et Cie 1927

2 BERNHARDT E Anat u phys Untersuchungen über den Nervus Depressor bei der Katze Med Disc Dorpat 1868

12 BEZOLD A v In Tigerstedt R Physiologie des Kreislaufes Berlin de Gruyter 1921 23

3 BRAEUCKER W Beitr z Klin d Tuberk 1927 66 1

BROCK Quoted by Danielopolu D in L'angine de poitrine et l'angine abdominale Paris Masson et Cie 1927

DE CYON F AND LUDWIG C Berichte der K Sachs Ges d Wiss 1866 Jour d An et de Phys 1867 4 472 Gesammelte physiologische Arbeiten Berlin 1888

4 DANIELOPOLU D L'angine de poitrine et l'angine abdominale Paris Masson et Cie 1927

FINKELSTEIN A Der Nervus Depressor beim Menschen Kaninchen Hunde bei der Katze und dem Pferd Arch f Anat Abt 1880 245

FRANCK F Signification physiologique de la resection du sympathetique dans la maladie l'epilepsie l'idiotie et le glaucoma Bull de l'Acad de Med 1899 41 565

HEINBECKER P Anatomic and physiologic criteria for surgical relief of cardiac pain J Thoracic Sur [illegible] 1932 33 [illegible] 517

HERING H E Die Karotissinusreflexe auf Herz und Gefasse Dresden u Leipsig 1927 Pfluger's Arch 1924 206 721

HEYMANS C BOUCKAERT J J AND REGNIERS P Le sinus carotidien G D [illegible] et Cie Paris 1933

HIRSCHFELD F G Angina pectoris saturnin Inaug Disc Berlin 1926 Zeitschr f klin Med 104

5 HOFER G Die chirurgische Behandlung der Angina Pectoris Wien klin Wchnschr 1924 3 [illegible] (July 10) 1924 1

KOCH E Die reflektorische Selbststeuerung des Kreislaufes Erg d Kreislaufforsch 1931 [illegible] Klin Wchnschr 1932 11 225

[15] KOSTER G AND TSCHERMAK A Über den Nervus Depressor als Reflexnerv der Aorta Arch f d ges Physiol 1902, *93* 24 Über Ursprung u Endigung des N Depressor u N laryngeus superior beim Kaninchen Arch f Anat u Physiol Anat Abtlg, Suppl 1902 255

[16] KREIDEMANN A Anatomische Untersuchungen über den Nervus Depressor beim Menschen und Hunde Arch f Anat u Physiol Anat Abtlg 1878 405

[17] MURRAY Quoted by Daniélopolu D in L'angine de poitrine et l angine abdominale Paris Masson et Cie 1927

[18] OSBORNE H Medical Times and Gazette 1862 *1* 317

[19] SAPPEY M P C Traité d anatomie desc, 1877 388 Paris V Adrien Delahaye et Cie vol 3 3rd ed

[20] SCARPA A Tabulae neurologicae ad illustrandam historiam anatomicam cardiacorum nervorum Ticini 1794 also quoted by Danielopolu D in L angine de poitrine et l angine abdominale Paris Masson et Cie 1927 Gesellschaft der Aertzte in Wien 20 April 1923 Wien Med Wchnschr 1923 *73* 891

[21] SCHWALBE C A Lehrbuch d Neur 2 Aufl in C I E Hoffmann s Lehrb d Anat d Menschen Erlanger E Bezold 1881 287

[22] TANDLER J Anatomie des Herzens Jena G Fischer 1913

[23] TESTUT L Traité d anatomie humaine 8th ed Revue by A Latarjet Paris G Doin et Cie 1928

[24] TIGERSTEDT R Physiologie des Kreislaufes vol 4 Berlin and Wien 1923 Lehrb d Physiol des Kreislaufes vol 2 W de Gruyter Co Leipsig Veit & Co 1893

[25] VANESCO E Quoted by Danielopolu D (6)

[26] VITI A Atti de la Soc Tosc di Science 1883 4

[27] WAGNER In Tigerstedt R Physiologie des Kreislaufes Berlin de Gruyter 1921-23

SECTION FOUR

Reference, Distribution and Simulation of Anginal Pain

CHAPTER X

The Dermatomes Concerned with Anginal Pain

For the mediation of referred anginal pain the visceral afferent fibers from the heart and aorta are brought into relation with somatic afferent fibers at a common entry i e the upper thoracic levels as a rule of Th1-Th4 on the left side We have already noted that the exact location of a common entry or locus of convergence is not definitely established According to some authorities the mediation and transfer of pain impulses is accomplished in the dorsal grey matter substantia gelatinosa Rolandii others again maintain that the mediation takes place in the dorsal ganglia or roots

The segmental myomeres of the body have an intrinsic reflex established early in embryonal life This reflex passes through the spinal cord well below the brain stem The reflex appears to be extra rather than intraspinal and is related probably to the dorsal roots The sensory supply to each trunk myomere (or dermatome) consists at least of three consecutive dorsal roots and in the case of limb dermatomes of about five dorsal roots This pluri segmental character of innervation persists even though in the case of the extremities the ring formation of myomeres is not easily distinguished

The usual or common dermatomes for anginal pain are supplied by nerves from Th1 Th4 levels occasionally C8 and Th5 are included This territory and its innervation are described The uncommon districts also with their innervations are delineated The special physiological and clinical considerations on the subject of referred pain are discussed in Chapters XI and XIII

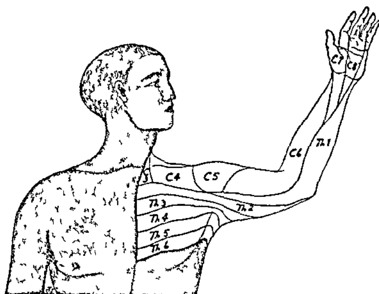


FIG 49 Ventral View This is a schematic representation of the anterior dermatomic segments from C 3 to Th 6 inclusive Of these only Th 1 to 4 and possibly C 8 and Th 5 are concerned with anginal pain as a rule The dermatomic segments on the thorax are a series of almost parallel girdle like stripes or bands encircling the entire thorax This pattern of segmental dermatomic distribution above the thorax is readily recognized when the human being assumes the quadrupedal position the segments running down the fore limbs instead of encircling them

In this illustration the left fore arm is raised and extended in order to show the arrangement of dermatomic segments on the ventral aspect of the hand forearm arm and shoulder in relation to those on the thorax

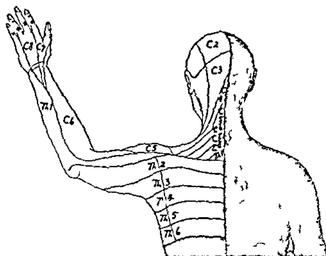
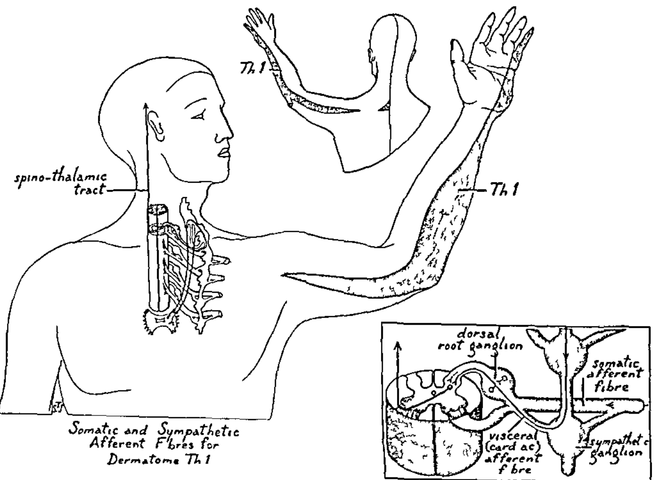


Fig 50 Posterior View This posterior view of the same region exhibits the same general arrangement It is of some interest that the dermatomic band of Th 2 3 4 and 5 segments are continuous as engirdling bands around the thorax whereas above this level all dermatomic stripes are interrupted and are followed from the posterior median spinal line on to the posterior aspect of the left arm only after skipping intervening areas belonging to other segmental cord levels



Th 1
spino-thalamic tract
Th 1
Somatic and Sympathetic Afferent F bres for Dermatome Th 1
dorsal root ganglion
somatic afferent fibre
visceral (card ac) afferent f bre
sympathet c ganglion

FIG 51

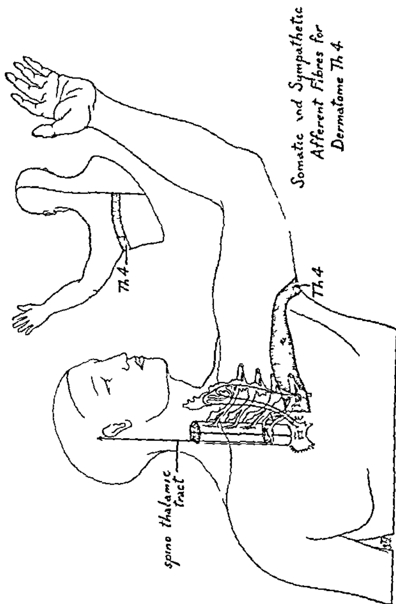

Somatic and Sympathetic
Afferent Fibres for
Dermatome Th 4
Th 4
Th 4
spino thalamic
tract

Fig 52

FIGS 51 and 52 The Spinal Cord Levels and the Dermatomes of Th 1–4 The relationship of the dermatomic surface areas supplied by Th 1 2 3 4 to the pathways of referred cardiac pain is illustrated in these drawings

The upper figure (Fig 51 p 188) is of the first thoracic level Afferent somatic fibres from the corresponding dermatomic surface in this instance from the ventral aspect of the forearm travel to the posterior spinal ganglion of the posterior division of the spinal thoracic nerve Within this ganglion a cell receives each centrifugal fibre and then sends forth a centripetal extension or fibre into the spinal cord This intraspinal afferent somatic fibre reaches a junction in the substantia gelatinosa Rolandii

A second pathway is necessary for referred pain This is made up of afferent sympathetic visceral fibres that leave the cardiac plexuses and ascend in the inferior and middle cervical cardiac nerves Passing unbroken through the stellate and middle cervical ganglia these fibres traverse the white communicating ramus of Th 1 and enter the posterior division (roots) of this first thoracic nerve Still uninterrupted the fibres enter the spinal cord and reach the junction *in the substantia gelatinosa already mentioned in connection with the somatic* afferent fibres The afferent visceral fibres from the cardiac plexuses to the spinal synaptic junctional zone are continuous and have no relay station

It is claimed that the substantia gelatinosa is the locus of convergence of somatic afferent and sympathetic afferent visceral impulses and that from this locus impulses are picked up by the spino thalamic tract and conveyed contralaterally to the thalamus and cortex These pathways somatic and sympathetic are the anatomic structures on which Martyn Hilton Ross Head and Mackenzie (for references see Chapter XI) built their cutaneo visceral conception of referred pain (see Chapter XI) Each dermatomic area is considered an external patch capable of announcing pain from a segmentally related insensitive organ in this case the heart

A similar description holds for the spinal cord segments of Th 2 3 4 etc for each segment there is a related dermatome (Fig 52 p 189 for Th 4)

The enlarged drawing (insert A of Fig 51 p 188) of the nerve structures at the Th 1 level for example enables the student to visualize the sympathetic and somatic pathways The afferent somatic fibre is represented as a dotted line the afferent sympathetic visceral fibre is drawn as a continuous unbroken line the spino thalamic tract is visible as a dark line ascending toward the thalamus

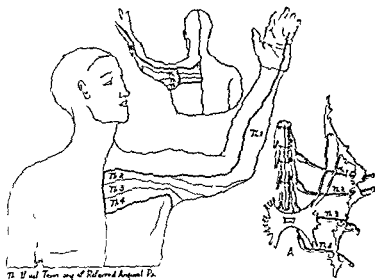


Fig. 3 The Usual Territory of Referred Anginal Pain This drawing is in the nature of an outline or map *of the dermatomic* area involved in the common distribution of referred anginal pain the area is sinistral as a rule it covers the cutaneous surface lying over the pectoral muscles and is continuous with *the ventral inner surface* of the left arm down to the web between the fourth and fifth fingers including *the ventral area of* the entire fifth finger

Referred anginal pain as a rule stays confined within the borders of this area There are however important and significant *exceptions The corresponding* posterior area is not drawn because singularly enough *posterior reference* of cardiac referred pain is comparatively uncommon

At A we have a diagram of the particular portion of the cardiac sympathetic innervation concerned with the referenc*e of pain and the* cutaneous *dermatomic* areas depicted above It *inc*ludes the spinal segments Th 1 2 3 *and 4 and* the corresponding spinal nerves which emerge from the spinal cord as ante*rior and posterior* divisions to unite and continue as one trunk beyond the corresponding s*ympathetic gangli*a Communicating white rami and grey rami connect each spinal nerve to its correspond*ing* sympathetic ganglion Only the middle and the inferior stellate sympathetic ganglia *are drawn* because it is generally accepted that sensory impulses do not reach the upper cervical ganglion

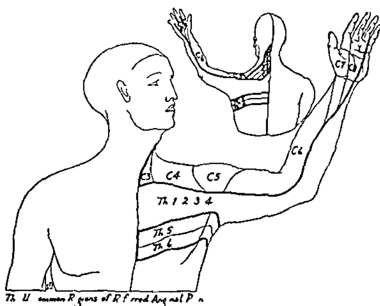


Fig 54 The Uncommon Territories of Referred Anginal Pain Above and below the dermatomic district into which anginal pain is commonly referred lie smaller areas The upper zone is supplied by the brachial plexus and upper cervical nerves C 2 3 4 5 innervate the surface area of the upper chest and shoulder region C 6 7 8 the ventral outer aspect of the arm The lower zone receives its innervation from Th 5 and 6 sometimes from still lower thoracic nerves These uncommon distributions of pain are far more often sinistral than dextral

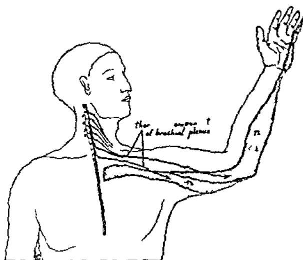


Fig 53 The Left Sympathetic Cardiac Innervation in Relation to the Brachial Plexus of the Same Side Only a small portion of the brachial plexus is commonly brought into relation with the nerve supply to the heart This small portion consists of the first and second spinal thoracic nerves which act as somatic pathways in the reference of anginal pain Other portions of the brachial plexus are known to participate in uncommon distributions of anginal pain (for fuller discussion see Chapter XI)

CHAPTER XI

The Distribution or Reference of Anginal Pain

PAIN that has its origin in the heart, coronary vessels or aorta is generally referred to other regions of the body and these regions are related to the heart by nerve pathways. The term referred pain as employed in this discussion signifies that pain is experienced in areas other than the sites of origin. In many cases it will coincide with referred pain as explained by Martyn,[35] Hilton,[27] Ross,[46] Head,[19] and Mackenzie,[31] and in other instances it will represent a distribution along routes not included in the description of these authors. We shall discuss the subject of referred pain under four headings: (1) the sites of its origin, (2) the distribution into the common territory through pathways which are well recognized, (3) the distribution into uncommon areas by pathways which are not so clearly understood, and finally (4) the characteristics of referred cardiac pain.

I Sites of Origin*

Pain is often centered in the heart or heart region and this includes the first or proximal, supraventricular, portion of the aorta. Some authorities have maintained that the point of origin, aorta or heart, determines the specific character and manifestations of the pain. Allbutt[1] and Wenckebach[58] argued that the aorta was the principal, if not the sole seat of anginal pain. Allbutt wrote that anginal pain was produced by irritation of the nerve endings in the first portion of the aorta, and Wenckebach, also Eppinger and Hofer[14, 15] and Hofer[21] emphasized the role played by the changes in blood tension within the aorta that affected the aortic or depressor nerve. This school correlated with anginal pain not only intra aortic alterations but primarily actual pathologic changes in the aorta itself.

However, the attempts to explain anginal pain on this limited basis proved unsatisfactory largely because many discrepancies were noted between the autopsy findings in the aorta and the antecedent clinical picture. Arteriosclerotic changes in the aorta were frequently not associated with pain; in rheumatic aortic disease pain was more often absent than present; and even in luetic aortitis anginal pain was by no means an invariable occurrence. The coronary vessels that supply the aorta were held responsible for the aortic changes that produced anginal pain.

* See Chapter XIII on the physiology of pain.

In an analogous manner the coronary vessels of the heart came to be regarded as the primary site of pain This point of view was of course not new (Jenner[9] had already written to Heberden[9] about the "ossification of the coronary vessels of the heart in angina pectoris and Parry[10] held the same view) and although it had much apparent validity it could not overcome certain objections It was observed for example that although many individuals with anginal pain had arteriosclerosis of the coronary vessels there were anginal victims without such involvement furthermore many of advanced age remained free of anginal pain though they showed pronounced chronic arteriosclerotic changes in the aorta and in the cardiac vessels

Since pathologic change in these structures so frequently failed to correlate with anginal pain or the rest of the syndrome of angina pectoris or acute myocardial infarction many observers concluded that the most probable explanation of the clinical manifestations of pain was spasm of these coronary vessels (Chapter XIII) Wenckebach contended that stasis and distention took place in the coronary vessels and that the distention produced pain or similarly that depressor reflexes in the coronary vessels brought on alterations in blood pressure in these vessels and so led to pain In these points of view the emphasis was on the physiologic not anatomic function of the coronary vessels and this emphasis still holds with respect to genesis of anginal pain and angina pectoris as propounded by later writers

The heart itself rather than the aorta or the nutrient coronary system came to be looked upon as the actual seat of the anginal pain The heart muscle of anginal sufferers is often damaged the extent and nature of the damage depending upon the nature and duration of the disease that attacks it Yet as in the case of the aorta and coronary vessels the myocardium may be markedly diseased and cause no pain Despite this the myocardial etiology found many adherents some of whom modified it For example Danielopolu has written that the metabolites of muscular action have a toxic effect and produce heart failure and pain also that anginal pain is an expression of myocardial impairment that follows from inadequacy of coronary circulation in the face of untolerated physical strain The cornerstone of the concept of anginal pain for nearly all students of the problem is the inadequacy of the coronary circulation and the ensuing effect i e anoxemia of the heart muscle (Chapter I)

From a practical point of view and our present knowledge it does not seem possible to localize anginal pain more accurately than in the heart or the region of the heart In many respects it would be of advantage to discover the exact point of origin of cardiac pain We have however until now not succeeded in doing so

Referred Anginal Pain

The mechanism and pathways of referred anginal pain are complicated and to comprehend them at all we must first have a clear understanding of the

CHAPTER XI

The Distribution or Reference of Anginal Pain

PAIN that has its origin in the heart, coronary vessels or aorta is generally referred to other regions of the body and these regions are related to the heart by nerve pathways The term referred pain as employed in this discussion signifies that pain is experienced in areas other than the sites of origin In many cases it will coincide with referred pain as explained by Martyn,[25] Hilton,[illegible] Ross,[46] Head,[19] and Mackenzie,[34] and in other instances it will represent a distribution along routes not included in the description of these authors We shall discuss the subject of referred pain under four headings (1) the sites of its origin, (2) the distribution into the common territory through pathways which are well recognized, (3) the distribution into uncommon areas by pathways which are not so clearly understood, and finally (4) the characteristics of referred cardiac pain

I Sites of Origin*

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* *See Chapter XIII on the physiology of pain*

of pain are then 'picked up' by the spino-thalamic tract and conveyed into consciousness as referred pain According to a large number of authorities th area of convergence this meeting place is established in the spinal cord a similar zone has not been discovered in the brain

It is known of course that anginal pain is often reflected into non cardiac usually peripheral or dermatome districts and that the reflection or radiation is achieved by the cooperation of somatic nerves that lead from dermatomes The connection between the integument of the body and the central nervous system is laid down in the early days of embryonal life a portion of the integument develops into the central nervous system and the skin itself never loses its neurogenic property This early intrinsic reflex between body somites including skin and the central nervous system below the brain stem persists during life and is the basis of referred pain into dermatomes The sensory innervation of each trunk myomere (or dermatome) consists of three adjacent dorsal roots and of about five dorsal roots in the case of the limbs We shall see that this pluri segmental arrangement has a practical bearing in studying clinical features of referred pain The capacity to experience referred pain in dermatomes is probably a biological endowment and exists in all likelihood in many species In man this type of pain together with intrabodily pain becomes a grim but beneficent danger signal There are occasions when the skin alone is the announcer of visceral pain

From Heberden s day if not earlier we have been confronted with the problem of explaining the mechanism of referred anginal pain As early as 1864 there is a clear description by Martyn[15] of referred cardiac pain and the pathways for it He recognized that upper thoracic spinal cord segments also sympathetic and intercostal nerves as well as dermatomic zones participate in the reflection of cardiac pain Inframammary pain is a referred neuralgic expression of some distress in the heart, he wrote A sagacious English surgeon Hilton[22] who was a contemporary of Martyn knew this also Ross[16] wrote on the same subject and argued for an irritable focus in the spinal cord where diffusion of referred pain took place Later Head[18] and after him Mackenzie[34] extended and developed the concept of referred pain It was Mackenzie who laid down the following premises as of major importance (a) viscera are insensitive to pain (b) dermatomes have their source of pain in a related organ and (c) the mediation of referred pain takes place as we have already commented in the spinal cord These premises however are open to challenge

Concerning the first premise it would not be accurate to leave the impression that Mackenzie may not have been aware of the inherent sensitivity of visceral organs As a matter of fact it was known to Ross in 1887 and to Head in 1893 that somatic pain from an organ differs from splanchnic pain e g within the very organ that is the source of this sensation Although Mackenzie must have known that organs are sensitive to pain he excluded th s as

nervous supply to the heart, coronary vessels and aorta This consists essentially of a vagal innervation arising in the brain stem supplying the aorta and heart and a separate sympathetic innervation *between the same cardiovascular* structures and the spinal cord At many points the vagal and the sympathetic nerves join anatomically, but this juncture does not mean that the impulses *carried by one system flow into the other*

The first to the fourth thoracic segments, sometimes the eighth cervical above and the fifth thoracic below, are the usual receptors for the visceral sympathetic nerves But the pathways of referred anginal pain include also somatic or peripheral fibers going to the same receptor zone The exact location of the mediation of referred pain is still unsettled, the dorsal grey matter, probably the substantia gelatinosa Rolandii, as well as the dorsal ganglia and the dorsal roots have been considered sites of mediation

Although it is held generally that afferent impulses from the heart coronary vessels and aorta travel by sympathetic and vagal routes the latter routes are not included in the usual reference of pain Indeed it may be questioned if the vagus is a significant afferent conductor of pain under any circumstances Yet although the existing proof is not entirely convincing it would not be wise to deny categorically in our present knowledge that the vagus is an afferent route From the smooth muscle of the intestines bronchi and similar structures the vagus is known to carry impulses of pain but a similar role for the other viscera including the heart, it seems to us is not so well established The *tenth cranial nerve in lower forms is a guardian and regulator of the gastro* intestinal tract and the heart In higher phyla, with the evolution of a separate breathing apparatus to meet the needs of a respiration carried on in free not dissolved *atmosphere the vagus develops nerves for the breathing organs* (Pike[41–43]) These newly developed nerves and other parallel evolutionary changes in the central nervous system are designed to control the mechanism of this higher type of respiration But here again the vagus is chiefly *guardian* or supervisory in character and conduction of pain is not part of its function To a great extent a similar evolutionary process is followed by the vagus in connection with the heart the nerve assuming and exercising chiefly if not wholly a regulatory function

The sympathetics, on the other hand are unquestioned conductors of pain Cardio aortic impulses of pain ascend in sympathetic fibers that converge upon the left upper thoracic levels of the spinal cord in the dorsal grey matter probably in the substantia gelatinosa Rolandii Here afferent somatic neurons from related dermatomic zones also converge Impulses of pain, therefore that originate either in the heart coronary vessels or the aorta and those from the dermatomic or surface areas supplied by the spinal nerves of the upper thoracic region, Th 1 to Th 4 triangulate so to speak upon common points of convergence in these four levels and in these levels it is claimed the mediation of referred pain takes place From these common loci, sensations

the dorsal grey matter probably in the substantia gelatinosa Rolandi of the upper thoracic spinal cord levels This hypothesis dominates the literature on the subject As the theory stands however it has to overcome important objections To begin with and as far as can be ascertained no one has defined anatomically the central connections for pain as exclusively in the entry zone of the dorsal grey matter of the spinal cord (Chapter XIII) Pike[41-43] in this country and Danielopolu[3] in Romania have suggested that the mediation of reference is quite likely to be extraspinal According to Pike the concept of an intraspinal mediation ignores the observation that referred pain is nearly always radicular in character and this type of distribution could hardly be inaugurated within the cord where impulses would be expected to undergo diffusion through several segmental levels by plurisegmental connections Pike feels that the actual mediation may be accomplished by a transfer of impulses or their effects from afferent visceral to afferent somatic fibers both types of fibers in the dorsal root lying juxtaposed and without myelin sheaths

Another objection to the theory of mediation within the spinal cord is based on the fact that the common neurons in the cord receiving a converging group of sensory impulses from multiple foci on the surface of the body, frequently fail to produce anginal pain This renders it difficult to accept uncritically that the general difference in the acuity and in the localization of referred pain and of touch derives from the circumstance that touch sensations are carried by fibers each of which makes a contact with an individual central neuron whereas the impulses of painful sensations transmitted along multiple fibers converge upon a common central neuron

Recently Morley[37] in England has expressed his reluctance to accept the Ross[46] theory of the mediation of pain based on a diffusion in an irritable focus in the spinal cord Danielopolu had already published several articles on the subject of extra spinal mediation With Hristide[13] in earlier publications and again in 1938[3] alone he viewed the meeting point of somatic and visceral afferent neurons as an articulation situated in the posterior spinal ganglia and he believed this junction could be disturbed by severing the somatic neuron He cut the intercostal nerves from Th 1 to Th 4 leaving the visceral afferent fibers intact This brought relief and abolition of pain a result confirmed by Lemaire[29] according to Danielopolu The underlying principle of this method would seem to be akin to that at work in the procedure of Weiss and Davis[8] who relieved sufferers of referred pain by locally anesthesizing the related and involved skin dermatomes Both methods are designed to lessen the number of somatic afferent impulses of pain delivered to the synaptic junction (or dorsal roots) The result of such a reduction might be explained on the ground that referred anginal pain is caused by a summated effect of charges of energy metabolic or electrical transmitted along the afferent somatic and visceral fibers and that the necessary quantitative threshold for this effect is unattainable when an adequate number of somatic sensory impulses are elimi

having no part in the mechanism of reference and went even further by saying that all visceral pain is referred. The ability of an organ to "feel" pain was held as an activity separate from its capacity to project pain into cutaneous areas of the body. While the viscero cutaneous theory of Mackenzie helped clarify many aspects of visceral referred pain and was of special use in accounting for intense surface pain and the occurrence of hyperalgesia of the skin with sudomotor, pilomotor, and vasomotor manifestations, the theory failed to recognize that the cause of a peripherally distributed pain is to be sought often in a local peripheral lesion and that pain has other than a single possibility of reference into related dermatomes. Furthermore, in Mackenzie's scheme there was no room for the possibility that pain of one viscus may be transferred into other viscera.

Beginning with Hurst's[3] observation in 1911 on the pain of hollow viscera a growing mass of experimental and clinical evidence and a closer analysis of the mechanism of referred pain strengthened the belief that viscera themselves are often the sites of pain and that dermatomic pain is not the sole expression of visceral referred pain. These studies demonstrated also that it is fallacious (Chapter XIII) to draw inferences of visceral insensitivity from the effect of artificial extraneous trauma, it is essential for the experimental injury or stimuli to be more nearly of the same nature and magnitude as those that naturally induce pain, i e obstructions in hollow viscera, increased tension beneath a tight capsule of a solid organ, augmented tension in the muscular layers of blood vessels. These kinds of stimuli are frequent and natural occurrences and induce pain in the organ affected. Similar deductions hold for the heart, and the following observations bear witness to the inherent sensitivity of various organs and structures. Pain results from contractions of hollow organs (Hurst,[3] Schrager and Ivy[49] Pollock and Davis[44] Ashkenaz[3] Ryle[47,48] Goldscheider[16–18]). The intravascular injection of sodium iodide produces visceral arterial pain (Moore, Moore and Singleton[36]). Leriche[30] also Livingston,[33] produced pain by crushing arteries, while Odermatt,[38] also Spiegel and Wassermann,[54] found that distending the larger arteries notably the aorta was painful. Sutton and Lueth[56] developed proof that an abrupt anoxemia of heart muscle precipitated heart pain.

The second premise namely that dermatomes have their source of pain in related organs while a useful hypothesis and in agreement with many if not most examples of peripheral radiations is too inclusive. Obviously it is stronger than coincidence that anginal radiations are nearly always sinistral yet this does not exclude the existence of local lesions to account for peripheral pain in these parts. Indeed, peripheral nerves blood vessels or lymphatics may have such lesions that come to light only after long and diligent search. This aspect of the problem has been emphasized in the critical observations of Hilton[illegible] Pike,[41–43] and Livingston[33]

The third premise of Mackenzie[31] assumed that the reference is mediated in

The radiation often fails to cover all of the usual area outlined above but any portion experiencing pain or any other sensory disturbance will form an orderly pattern in accordance with the nerve distributions There are therefore in most cases no isolated bizarre or unrelated patches of painful sensation The general rule is that radiation follows the course of nerves and blood vessels and this radiation is radicular in type and therefore related to the nerve roots The pain is seldom of the diffuse type that is related to the nerve trunks but when it occurs it assumes the characteristics that belong to diffuse pain and not the patchy distribution of the radicular variety

Whereas in most instances the distribution is a left sided unilateral one very occasionally it is right sided or else bilateral These atypical distributions need not be too disconcerting a factor in making a correct diagnosis since the other aspects of the anginous picture will ordinarily confirm it Further more diagnostic perplexities will be solved if in right sided pain the history or the character of the illness will lead one to uncover lesions on the right side of the body for example right supra or infra-diaphragmatic troubles In the case of bilateral chest pain extending into both arms confusion with anginal pain exists when there are overlapping clinical features attributable to disorders of structures like the spinal cord spinal nerves or inflammation or tumors of chest viscera As a general rule but this is not always a dependable matter the anginal pain is recognized even when it is referred to the right or to the right and left by its pecial characteristics viz the character of the pain, the angor animi etc These unusual distributions therefore as well as the absence of distribution and the absence of centrally localized pain do not necessarily militate against arriving at the correct diagnosis of anginal pain

The right sided distribution as well as the bilateral are similar to left sided distribution in this important respect namely that all three are limited to the sympathetic and somatic nerve supplies that converge upon the 1st to the 4th thoracic levels the vagal supply as we have already observed probably taking no or a subordinate part The right and bilateral spreads are limited to areas that are supplied by the pinal cord at levels corresponding to those that deal with sinistral spread alone

III The Uncommon Distributions

The reference of anginal pain however is not confined always within these limits In addition to the more common left sided reference pain is known to move into contiguous areas above or below the usual territory, or into combinations of above and below (Figs 54 and 56) These comparatively uncommon zones may even be the sole areas registering pain

A The Upper Zone for Uncommon Radiation

The upper zone comprises the head scalp face neck the supra and infra clavicular regions the shoulder and the ventral aspect of the arm including

nated or blocked (Chapter XVII) On the basis of careful experiments on dogs Spiegel and Hashimoto[53] reached a view contrary to Danielopolu's According to these investigators, "pain from the stellate ganglion could still be produced after the degeneration of the corresponding somatic elements of the spinal ganglia" (Spiegel) *

II The Common Territory of Reference

From its locality, the heart or the region of the heart,† the left precordium, or the anterior chest wall of the left side, pain spreads into a well recognized area This area as a rule, is confined within well defined borders (Fig 53) With the left arm extended at right angles to the chest, this region forms a band, broader at the midsternum where it extends from the 3rd or 4th to the 6th and 7th intercostal spaces It continues anteriorly outward across the upper axilla, almost bisecting the ventral aspect of the arm and remains *limited to the inner area, narrowing rather suddenly as it approaches the* wrist to taper off on the ventral surface of the fifth finger In actuality dermatomic areas are not defined as sharply as in this description

Except for a small axillary territory this area is almost entirely ventral and practically always sinistral The posterior divisions of the left 1st, 2nd, 3rd and 4th thoracic nerves also supply a similar posterior dermatomic area of the chest This posterior surface, however seems to be as a rule untouched by pain ‡ This is an interesting phenomenon and is, perhaps, a practical point in the differential diagnosis of anginal pain In most cases pain is substernal or close to the sternum next in frequency is involvement of the left pectoral region but spread and diffusion of pain can augment or supplant the more *circumscribed localization Accordingly, the pectoral region and the inner* surface of the arm down to the fifth finger may pain and smart while the deep pain in the heart is still present or has subsided The radiation into the pectoral region is through the lower cervical and upper thoracic nerves the pectoral muscles receiving their supply from C 5, 6 7, 8 and Th 1 The radiation into the left arm passes along the 1st and 2nd thoracic nerves the former supplying chiefly the inner aspect of the upper arm Both these thoracic nerves are part of the brachial plexus and in this way this particular part of the plexus shares in the propagation of anginal pain (Fig 55) As this propagated pain subsides or disappears the cutaneous areas are left numb or tingling or "weak" Sometimes this is not the rule tenderness to pressure is elicited along the nerves which conveyed the pain the ulnar and the four intercostal nerves

* Personal communication

† For the purpose of this discussion the coronary vessels as a seat of anginal pain are included when the heart is mentioned

‡ Danielopolu says pain into the back is frequent but he seems to mean thoracic pain as in thoracic visceral disease and not cutaneous manifestations

the first four fingers Into these areas with a few exceptions to be noted, pain is transmitted by accessory sympathetic afferent fibers The exceptions are the neck and occiput, the cervical nerves of which are reached through the intervention of the vagus The rest of this entire region feels pain through the cervical plexus impulses of pain reaching the plexus through accessory afferent sympathetic fibers Heinbecker[34] found a limited number of cervical afferent sympathetic fibers and it is possible that these are already developed sufficiently in some individuals to act as an accessory route

Accessory Afferent Cardio-aortic Fibers

These accessory fibers in general are an anatomic endowment forming a pattern for each individual With regard to the heart and aorta the following groups (Fig 6) of fibers probably exist and the number and extent of their participation determine the distribution and the design of referred anginal pain especially into uncommon regions

(a) Afferent fibers in the cervical regions serving as white rami along which as White[59, 60] has suggested any cardiac afferent impulses that were carried would have to achieve a summation in the central nervous system before registering a sensation of pain

(b) Afferent fibers passing through the white rami of Th 5 Th 6

(c) Afferent fibers in the vertebral plexus entering the ansa Vieussens and connecting with the lower cervical nerves The presence of such afferent fibers is denied by Langley[36, 37] but accepted by Danielopolu

(d) Afferent fibers on the right side corresponding to the usual and uncommon groups of the left side The heart and aorta have a bilateral nerve supply and the right sided nerves could carry and localize painful impulses to the heart with or without radiation into the right side

(e) Afferent fibers passing between the vagal ganglia of the trunk and the superior cervical sympathetic ganglion

(f) Afferent pathways in the vagus trunk entering in the medulla

(g) Posterior rami from the 2nd 3rd 4th thoracic sympathetic ganglia to the cardiac plexuses containing afferent as well as efferent fibers

Any of the fibers of a b c e f and g may be predominant dextrally In most cases all the accessory routes are subordinate but when the usual left sided innervation is interrupted or destroyed as after alcohol paravertebral block for example any or all of these accessory pathways may take over the main burden of transmission of sensory impulses

Cephalic Distributions

The tracts that transmit pain into the head and intracranial parts the uppermost district of this upper zone are more difficult to comprehend The arrangement of somatic and sympathetic neurons described in connection with

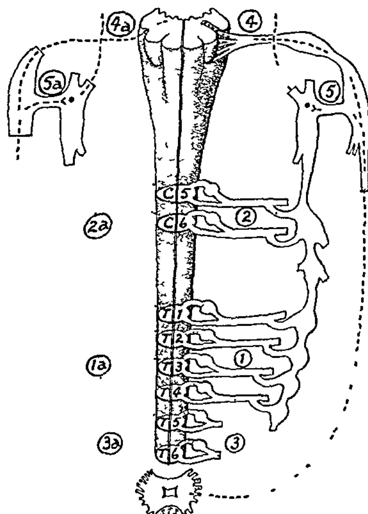


Fig 56 —A Schema of Groups of Afferent Fibres Capable of Transmitting Referred Anginal Pain 1 represents the usual well recognized sinistral group entering the Th 1–4 cord segments through corresponding white rami (1a) is a similar dextral group much less frequently involved 2 represents upper left cervical fibres going from upper cervical ganglia to corresponding cervical cord segments (2a) similar dextral fibres 3 represents lower thoracic fibres going from the lower thoracic ganglia to corresponding cord levels (3a) dextral fibres 4 represents the pathway of cardiac afferent fibres in the left vagus destined for the medulla (4a) a similar pathway on the opposite right side 5 represents the pathway of vagal cardiac afferent fibres that ends in the superior cervical sympathetic ganglion (5a) a similar pathway of the opposite right side 6 not included in the drawing is the posterior group of rami connecting the upper thoracic sympathetic chain to the cardio aortic plexus 7 also *not included* are the sympathetic fibres from the vertebral plexus entering the cervical plexus and sending communications to the ansa Vieussens The vertebral plexus is generally not accepted as an afferent pathway for cardio aortic pain

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referred pain that converges through the upper thoracic spinal cord or upper thoracic dorsal roots, is lacking here The superior cervical sympathetic ganglion by its upper prolongation, the internal carotid nerve develops an extensive intricate sympathetic network that follows the blood vessels and their ramifications and twigs, sending communications to the cranial nerves reaching special cranial sympathetic ganglia and in fact, supplying a vast variety of cranial structures This cephalic sympathetic system is, however supposedly entirely efferent and therefore, presumably not active in the distribution of anginal pain when referred to this "upper zone" Danielopolu maintains that afferent sensations pass along this cephalic sympathetic system but there are not many who concur Livingston,[33] too, claims that an afferent supply to the head exists and is evidenced by reactions of pain when, for example the middle meningeal artery is ligated In the absence of afferent sympathetic fibers[45, 55] we are hard pressed to explain satisfactorily why anginal pain and related manifestations are felt in head structures We present several possibilities

(a) The cranial nerves act as afferent pathways Although the cranial nerves bear a certain analogy to spinal (somatic) nerves they fail in general to fulfill the role played by the latter as an arc for referred pain The sensory component of the fifth nerve transmits anginal pain and it is quite possible that the tenth, seventh, and ninth do so also In the case, at least of the sensory component of the fifth nerve, vagal fibers intersect it (Fig 57) and in this way inaugurate pain and other features in the head A sensory component of the seventh nerve provides a pathway for deep sensation from the face and a sensory component of the ninth nerve does the same from the posterior third of the tongue and from the pharynx

(b) Cranial sympathetic (efferent) fibers register anginal pain in the head region In the absence of cranial afferent sympathetic fibers and since head structures are known to experience pain, Pollock and Davis[41] developed the hypothesis that pain in the head region is the result of sympathetic motor (efferent) effects upon the skin and blood vessels in this region Similarly Penfield[40] asserted that referred anginal pain into the head depended upon the action of cranial efferent sympathetic fibers He accepted the assumption that *the vagus and its depressor nerve carry afferent impulses of pain* to the superior cervical sympathetic ganglion Within the ganglion efferent cells are stimulated and inaugurate efferent impulses along cranial efferent sympathetic fibers (Fig 58) In this way a reaction is registered in the vessels of the head and localized sweating (also in the face and neck) and other manifestations appear e g a general rise in blood pressure and perhaps even spasm of the coronary vessels

The foregoing was the actual course of events in a patient reported by Penfield with luetic aortitis and severe angina pectoris in whom the middle and inferior (stellate) ganglia were removed on both sides thus isolating the supe

nor ganglia Nine days afte the operation the patient developed pain which started around his neck like a collar spreading into the gums and to the top of the head Perspiration covered both sides of the forehead and the systolic blood pressure rose to over 300 This effect, according to Penfield [10] was the result of a reflex within the autonomic system I enf eld points out that similar

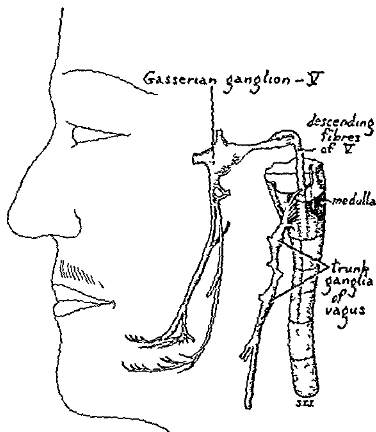


Fig 5/ The Vagal Aff e t Fibres From the Heart to the Me lu la These fibres are observed ascending in the vagus tr nk to the trunk ganglia then entering the me lulla where they ntersect the e sory limb of the th e anial nerve In this way anginal pain coul l be referred into the district supplied by this portion of the 5th nerve

reflexes are encountered in other areas of the body and are known as axon reflexes (Sokownin reflex) described by Langley [6] [7] and by Langley and Anderson [?] Invoking this reflex as the sole bas s for referred anginal pain to the head however fails to recognize that sensory impulses in the vagus nerve need not lea e it for the sympathetic system but are free to go to the medulla directly there to reach cranial nerves and perhaps other structures

Whereas in the case of the distribution of pain along the sensory component of the fifth cranial nerve we hold responsible a mechanism that depends upon the intervention by the vagus or intervention by cranial efferent sympathetic

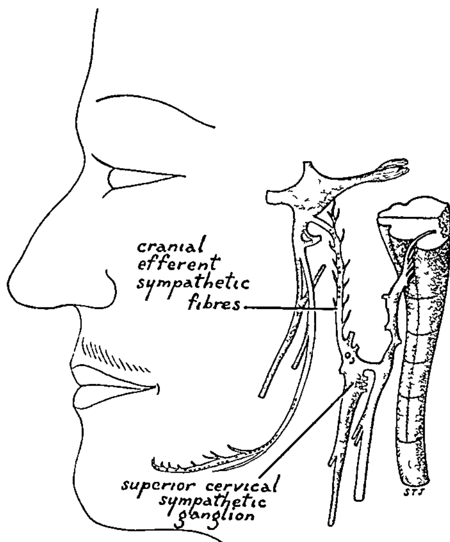


FIG 58 —Vagal Afferent Fibres to the Superior Cervical Sympathetic Ganglion (The Autonomic Reflex (Sokownin) in the Vagus) From the cardiac plexuses afferent fibres ascend in the vagus and cross into the superior cervical sympathetic ganglia In these ganglia efferent (motor) cells are supposedly stimulated to set off efferent effects along cranial efferent sympathetic fibres and into cranial nerves of which the sensory component of the fifth nerve is an example

fibers in the case of other cranial nerves, for instance the seventh and ninth, we are forced to explain their involvement without any intervention of the vagus and upon the action of efferent fibers only

(c) The cephalic manifestations are an expression of a Ritter Valli reaction The induction of post-operative pain and other sympathetic features after extirpation of cervical ganglia as observed for example in Lenfield s case may have a totally different explanation namely the Ritter Valli reaction According to this, an excitatory stage follows the severence of a nerve and physiological effects specific for this nerve continue until degeneration of the peripheral nerve sets in whereupon its physiological action is abolished The phenomenon however has a bearing only during the early weeks after injury to the nerves

The Vagus Nerve as a Route for Anginal Pain

The opinion and reasons to support it have already been expressed that the vagus nerve is perhaps a subordinate or inconsequential conductor of anginal pain There exist nevertheless a number of clinical instances where the anatomic course followed by the vagus and the location of its anastomoses to other nerve structures and systems (Fig 52) would best explain the occurrence of atypical radiations The vagus nerve therefore is included in this text as a possible route for anginal pain

Through the vagus nerve sensory impulses are supposed to reach the back of the head along the second and sometimes the first rudimentary cervical nerve (Danielopolu) or the ear through the second cervical nerve The jugular ganglion of the vagus in the jugular foramen gives off an auricular branch which supplies the external auricle the bony portion of the external auditory canal and the lower part of the external ear drum Through this nerve anginal pain may lash any of these structures and by some this nerve is held responsible for similar pain in the side of the neck arriving through the third cervical nerve and for pain tenderness and hyperalgesia at the points of insertion of the trapezius muscle and even through lower cervical nerves to other neck and shoulder muscles Furthermore by its connection with the fifth cranial nerve as already described the vagus carries referred pain into the lower jaw or into the teeth Vagal together with sympathetic fibers form an extensive thyroid plexus the sympathetic fibers run to the middle cervical ganglion the vagal fibers to the laryngeal nerves Although manifestations of referred pain through this plexus are not established it is possible that a disturbance, as after thyroidectomy of this plexus as well as of the superior and middle sympathetic cardiac nerves close to the posterior surface of the thyroid gland contributes to the alleviation of anginal pain The tenth nerve is also a sensory nerve to the pharynx esophagus and to the stomach and lungs

The vagus also has motor nerves for the palate pharynx trachea esophagus and lungs The motor branches to the pharynx transmit the horrible gripping spasm to the throat a fairly common and extremely distressing manifestation during an anginal attack and not to be confused with the sensation of suffocation This pharyngeal spasm allegedly is more frequent in anginal pain of

aortic origin The motor component of the tenth nerve also supplies the stomach and duodenum, and referred pain into these organs is not rare The spinal accessory nerve has sensory but also predominantly motor fibers which join the vagus at its nodosal ganglion, but these accessory motor fibers have no great significance

Nearly all authorities agree that sensory sensations from the heart or aorta cannot reach the sympathetic system above the level of the middle cervical ganglion The upper cervical sympathetic trunk contains no afferent cardio aortic fibers, and although Heinbecker found that the superior sympathetic cardiac nerve transmits sensory impulses, these are destined for the vagal ganglia In any event interruptions in the sympathetic system above the middle sympathetic ganglion in all likelihood, and above the superior ganglion unequivocally would have to bring high cervical afferent sympathetic fibers or the vagal system into action to permit the registration of pain in the uncommon areas innervated by the left cervical nerves or by cranial nerves The vagal route is not necessarily reserved for emergencies as in Penfield's post operative case it is supposed to function as we have already intimated even when the cervical sympathetic system is intact providing an ascending tract for afferent impulses

B THE LOWER ZONE FOR UNCOMMON RADIATION

In contrast to the upper zone, the lower zone for the uncommon registration of anginal pain is much less clearly understood Generally speaking, the reference of anginal pain into these lower regions, i e below the level of the 4th or 5th thoracic spinal cord segment is less frequent than upper radiations The lower reference has a special interest and significance, however, in connection with the reception of pain into abdominal or pelvic regions where anginal pain would seem improbable and where extra cardiac disease either obscures the true nature of the malady or vicariously and misleadingly takes on the clinical form of heart or aortic pain In exceptional cases, pain from the cardiac and aortic plexuses possibly passes through the lower thoracic intercostal nerves as far down as the 5th less likely the 6th, sometimes even as low down as the 12th, and, corresponding zonal bands or stripes on the left chest innervated by these intercostals become the dermatomic sites of referred pain, their pathways somatic and sympathetic, are identical with those found in the upper thoracic levels

Clinical Examples of Atypical Radiations

Anginal pain can have very unusual radiations With a knowledge of the accessory groups of afferent fibers these clinical occurrences are more readily followed and better understood

Reliable observers have described puzzling radiations to the left shoulder

with or without radiations to the rest of the limb (Edeiken and Wolferth[12] Libman[3] Boas and Levy[3]) The mechanism for this in our opinion is similar to that in the case of other peripheral radiations In the presence for instance, of a peripheral lesion at the shoulder afferent impulses that originate in it

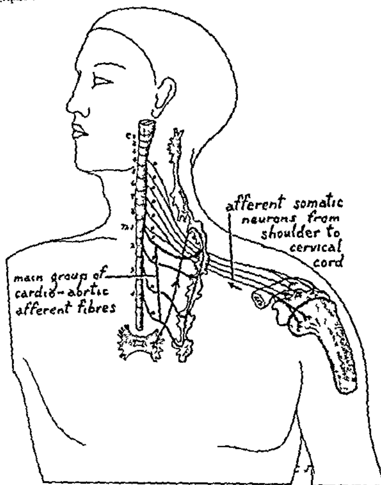


Fig 9—The Routes for Referred Anginal Pain to the Shoulder The afferent somatic neurons from the shoulder may enter the spinal cord by accessory fibres as low as the 1st or even 2nd thoracic levels a region which receives cardiac afferent impulses Anginal pain could thus be referred through the lowermost (accessory) somatic neurons into the shoulder

would find an entry not only into the spinal cord or dorsal ganglia at the levels of C 4 5 6 but also into the upper thoracic levels by means of accessory somatic fibers travelling through lower cervical or upper intercostal nerves (Fig 59) But even in the absence of a peripheral lesion at or near the shoulder this

region and its surrounding tissues would be capable of acting as the equivalent of a dermatomic area or as the equivalent of an extra cardiac organ or structure *The shoulder, therefore is able to feel referred impulses from the heart,* either by the route already described in connection with a peripheral lesion in

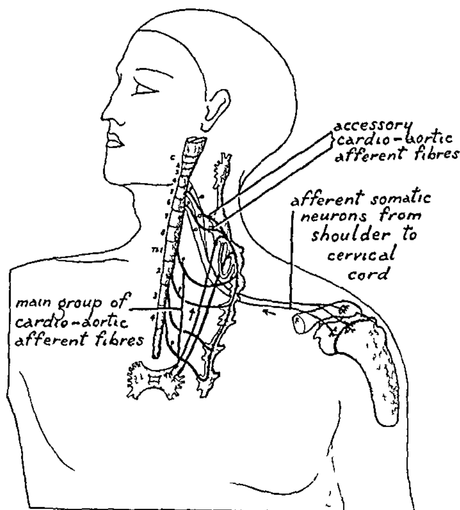


Fig 60 —The Routes for Referred Anginal Pain to the Shoulder The 4th 5th 6th cervical nerves connect the shoulder to corresponding cervical segments of the spinal cord Visceral afferent fibres from the cardiac plexus reach the upper thoracic segments Th 1-4 of the spinal cord by means of corresponding upper thoracic white rami In this drawing a group of cervical rami is portrayed that would be capable of carrying afferent impulses from the heart into *those cervical cord segments that receive afferent neurons from the shoulder* Anginal pain could thus be referred into the shoulder

this neighborhood i e through accessory somatic neurons or through the intervention of accessory cervical sympathetic fibers (Fig 60) such accessory fibers as we have already observed have been described by Heinbecker [1]

Other illustrations of the possibility of transmission of painful sensations by

means of accessory sympathetic afferent fibers are not lacking For instance a case of severe anginal crisis relieved by surgical attention to a postoperative stump in the left arm (Aronowitsch) the persistence of pain after many dorsal spinal nerves were cut (Spiegel[31, 32]), pain from peritonitis after a high transverse myelitis (Livingston[33]) the distribution of pain into a subacromial bursa after a coronary thrombosis (Libman[illegible]), and anginal pain referred to a carious tooth (Mackenzie[34]) The projection of anginal pain into abdominal viscera also constitutes an example of the functioning of numerous visceral afferent fibers in addition to the more common groups that pass through the upper left four thoracic levels To this last problem the propagation of pain from one organ into another we now turn

In all these references we have postulated the existence of a pattern of afferent pathways wherein impulses from the heart coronary vessels or aorta and from non-cardiac regions converge upon the dorsal grey matter or dorsal roots concerned with heart pain This pattern is an anatomic endowment so to speak and it may exhibit individual differences in its multiple or localized predominance of entry into the spinal cord

The Reference of Anginal Pain to Noncardiovascular Viscera

In an attempt to understand the mechanism and follow the pathways of referred anginal or any other type of cardiac pain to regions that are related to the spinal cord below the lowermost level described thus far in this text Th 5 or 6 we are led to believe that afferent impulses in the ganglionic trunk descend to this level also lower To accept such a postulation however has seemed unsatisfactory and unwarranted It has been argued in the first place that no proof exists that cardiac impulses of pain descend so low in the sympathetic trunk and in the second place even if there were such evidence we would still be confronted with the difficulty of knowing what eventual destination such impulses could have except to enter corresponding spinal cord levels where if perchance afferent tracts were hit nonradicular peripheral references would follow instead of the radicular type actually seen in cardiac referred pain

Similar and other objections have been marshalled in connection with the distribution of cardio-aortic referred pain into organs other than the heart This type of reference has been ascribed to a mechanism of peripheral distribution basing such an explanation on the well known phenomenon that pain is announced at or referred to the end of the peripheral distribution of an afferent nerve regardless of the site of the lesion or excitation along that nerve In the domain of the somatic nervous system an excellent example is the pain brought to the knee along the obdurator nerve that is initiated at the hip as from tuberculosis of the hip But strictly speaking, this is not referred pain in

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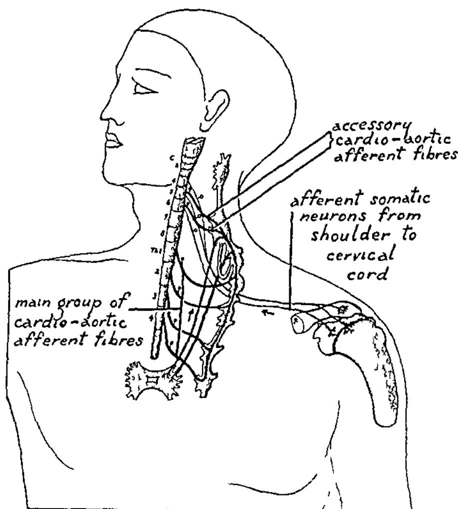


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the sense of the term applied to referred visceral pain The impulses of pain along the obdurator nerve undergo no mediation in any locus of convergence It would be well, therefore, to omit the use of the term "referred pain" for manifestations of this kind

Referred cardiac pain, in contrast, depends upon a summated effect between converging streams of impulses that arrive at a zone of mediation or transfer According to this concept, cardiac impulses at the upper thoracic levels are supposed to initiate referred pain along tracts or fibers with which they come in contact in the spinal cord or in any other locus of convergence With regard to the projection of cardiac pain into some other organ, a sensory disturbance *in the heart would be transmitted to the central nucleus of a fiber that carried* this impulse of disturbance and would be referred into a peripheral distribution other than the heart In other words, afferent impulses of cardiac pain on reaching the spinal cord (or the dorsal roots or ganglia) may terminate in the cord or medullary nucleus of a nerve that receives afferent fibers from some other unrelated viscus

The Propagation of Referred Pain from One Viscus into Another

There is in our opinion an explanation of the propagation of referred pain from one viscus into another which is in harmony with the known anatomic, physiologic and experimental facts Considerations of referred anginal pain bearing upon its distribution to various abdominal viscera and vice versa abdominal visceral pain referred to the heart, as well as other relevant material will be more clearly grasped, we believe, after the discussion of this explanation The concept of a mass action of the entire autonomic nervous system is an essential part of this discussion for the rest we hold that all abdominal organs pelvic and thoracic probably as well possess multiple afferent anatomic pathways that may enter practically all the dorsal spinal roots and through these multiple afferent fibers as we shall attempt to show anginal and abdominal visceral references are mediated

The Multiplicity of Visceral Afferent Pathways

We alluded to the difficulty of understanding the pathway of visceral afferent sensations that reach dermatomic levels and viscera connected to the spinal cord below the 5th or 6th thoracic levels This however is an example of but one part of the problem The other is to account for the registration into the heart and its vicinity of pain that arises in distant organs or other non cardiac structures (Fig 56) To illustrate a paroxysm of anginal pain due to an abrupt coronary occlusion occasionally simulates acute *gall bladder or pancreatic dis*ease or sudden perforation of a peptic or duodenal ulcer and the pain and its references are located below the diaphragm, even penetrating into the pelvic region Conversely the pain of any of these abdominal or pelvic conditions is

focused in the heart and its immediate neighborhood and even overflows into the brachial and cervical plexuses We have then clinically bi-directional references and with the heart as the focal point, the registration is centripetal or centrifugal This state of affairs raises the suggestion that mediation after all, may be intraspinal and accomplished by intraspinal collaterals connecting the somatic and sympathetic systems The clinical storm' so often an accompaniment of anginal pain is probably governed by higher centers most probably in the medulla diencephalon and cortex Indeed without laboring the point an abrupt thrombosis in a heart vessel or a sudden perforation of a peptic or duodenal ulcer or of an intestine may prove to be expressions of very similar excitations stemming from common regulatory centers (see Cushing[7] Peptic ulcers and the interbrain) and with a certain cogency therefore we may speak of angina pectoris of the gallbladder of the pancreas and so forth

On anatomic as well as physiologic ground the occurrence of centripetal tran mission of pain along commonly shared visceral afferent fibers secures a new and strong support in the recent work of Ashkenaz[3] on the centripetal visceral pathways of the gallbladder in the cat Ashkenaz and Spiegel[1] in an earlier publication described in the cat a contraction of the panniculus carnosus muscles which produces a movement of the skin of the trunk on the underlying tissues This contraction is caused by a spinal cord reflex after painful disten ion of the gall bladder or duodenum and the reflex has its afferent pathway through the splanchnic nerve its efferent pathway through the anterior thoracic nerves and the central part of the reflex arc is located within the pinal cord

Utilizing this localized muscular contraction viscero-panniculat reflex as a signal of pain Ashkenaz[3] plotted out the distribution of afferent visceral fibers from the gall bladder and he determined that these fibers go to practically all the right sided thoracic dorsal spinal root ganglia the upper level was Th 2 the lower level Th 10 as a rule but the lower level was not as sharply defined as the upper in some cases reaching as low as Lumbar 3 He found furthermore these visceral fibers pursue either of two ascending routes i e they ascend in the sympathetic trunk before entering the spinal cord or enter the spinal co d at a low level and ascend by intraspinal paths Last but equally important the afferent visceral fibers may cross from the right sympathetic trunk to the left trunk in at least one animal of the 60 cats studied afferent visceral fibers entered a number of thoracic dorsal roots on the left side Before this Schrager and Ivy[49] and Davis et al[16] had called attention to the large number of afferent connections in the case of the gallbladder with many dorsal roots Ashkenaz s investigations however are most complete and have the virtue of having utilized a single well defined and objective signal of pain subject to no misinterpretation

The Predominance of Entry of Visceral Afferent Fibers into the Spinal Cord

This bilateral, although predominantly right sided, sympathetic innervation and the arrangement of a series of multiple entries into many dorsal roots bear

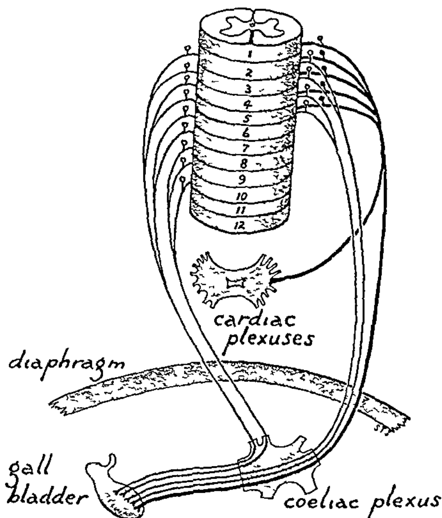


FIG 61 —The Pathways for Referred Pain from the Gall Bladder into the Cardiac Territory The gall bladder has many afferent fibers entering almost every level of the thoracic cord on the right side and a number of upper levels on the left side as well The cardiac afferent fibers have their usual entry into the upper four thoracic segments of the left side The radiations of gall bladder and heart disease are therefore as a rule distinctly apart and registered in characteristically different areas of the body When gallbladder pain is referred into the cardiac territory we may explain it on the basis of an arrangement of fibers illustrated above The predominance of entry of afferent fibers from the gallbladder is indicated as on the *left* side of the upper thoracic cord the zone in which anginal referred pain is mediated The same scheme would hold if the mediation were in dorsal ganglia or roots

directly upon our problem of referred pain in man Since there is every reason to believe that a similar arrangement exists for him, it would appear that if

the entry of visceral afferent impulses from the gallbladder were predominantly high this would correspond practically to the level concerned with heart pain (Fig 61) (It is conceivable that the usual and predominant right sided development of afferent fibers from the gallbladder might be reversed

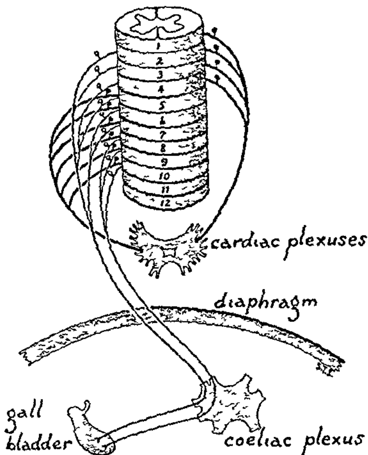


Fig 62 – The Pathways for Referred Anginal Pain into the Gall Bladder Region The drawing illustrates the arrangement of afferent fibers that would prevail in those comparatively infrequent cases when anginal pain is propagated into the gallbladder region

The cardiac afferent fibres are drawn here as predominantly dextral and overlapping the entry zone of the main group of afferent fibers from the gall bladder

with a left sided predominance in this type of case) A similar multiple arrangement for the entry of afferent impulses to all or very many dorsal roots probably exists for other abdominal viscera This would render it possible to have painful impulses pass from noncardiac organs to local or referred areas in a

about the heart and pain could be projected out of an involved organ, where it properly belongs, into the heart or aorta

On a similar anatomic basis the probability lies open that visceral afferent impulses from the heart are carried, in some cases, to dorsal roots below Th 4 and even below Th 5 or 6, furthermore, similar fibers may find an entry into the spinal cord through a number of dorsal roots on the contralateral (right) side If the entry of afferent heart impulses were predominantly low, below Th 6 or 7, or fortuitously coincided with those segmental cord levels receiving visceral afferent fibers from abdominal and pelvic viscera, anginal pain might very well be experienced in the related noncardiac viscera (Fig 62)

The pathways for simulating anginal pain in or away from the heart, depend therefore, upon the architectural pattern of the visceral afferent pathways from the heart and all other organs or structures With regard to peripheral structures as instigators of pain referred to the heart, the afferent somatic nerves may be regarded as analogous to the visceral afferent fibers with this exception that somatic nerves enter a fixed number of related cord segments, at most, three to five The references of pain, therefore, cannot be as widely ranged as in the case of the visceral afferent pathways A case in point is the intense pain of brachial neuritis known to extend to or center in the heart region and simulate anginal pain (Lian,[31] also Boyer[6]), but the sensory impulses cannot reach more than the upper thoracic, possibly the 8th cervical spinal cord segments or corresponding dorsal roots, and within the spinal cord these impulses travel up or down for only a few levels by either somatic or sympathetic dendrites as the case may be

IV Characteristics of Referred Anginal Pain

Many of these characteristics, already mentioned are here regrouped and re emphasized

A Sinistrality

A striking aspect of referred anginal pain is its sinistrality and extention to the ventral chest wall and arm Although pain is known to penetrate to the back this is more likely to be a through and through deep pain reaching the vertebral column than a pain which is referred to posterior cutaneous areas in the left chest The most frequent type of chest radiation is transverse in direction but well into the left side, and is often an extension of the more centrally located substernal pain The involved area on the anterior chest includes not only the usual pectoral region but the left shoulder the entire neck, and the left arm as well or is confined to only one of these regions There are odd instances when the pain in the arm is limited in glove like formation to the ventral surface of the 4th and 5th fingers or the pain may form a bracelet encircling only the region of the left wrist Sometimes the left biceps muscle region is the seat of extremely sharp pain similar to the excruciating kind of a crushed

finger The spread into the head regions especially to the jaws teeth scalp and ear is not altogether rare and is apt to lead to much confusion and uncertainty in diagnosis Interesting observations are those of referred mandibular pain in teeth with caries or into a subacromial bursa etc Referred pain in the epigastrium in the flanks around the umbilicus and even lower in the scrotum or rectum is unusual but occurs In all these left sided radiation is predominant The right and bilateral distributions are much less frequent Danielopolu and Danulesco[10] observed right sided radiation in a case of complete situs inversus Whereas referred anginal pain is usually radicular in nature a number of the neurologic manifestations detailed above belong instead to the nerve trunk or diffuse variety

B Amplification

The attack of angina pectoris or acute myocardial infarction consists of physical and emotional upheavals The emotional elements do not concern us at this point the physical elements take the form of shock and other features among which pain is predominant and overwhelming The pain is a furious storm surpassed in severity by no other kind of pain This intense agony is often associated with anatomic lesions that are themselves disproportionately small to the havoc of pain they produce While there is not always a perfect correlation between the extent and degrees of anatomic lesion and the quality intensity and duration of pain the disparity in the case of anginal pain may be so striking as to call for some explanation

An attempt at an explanation is provided by the theory of amplification and summation developed by the studies of the electrophysiology of the nervous system It is claimed that evidence points to the summation of effects from the impulses of anginal pain that arrive at common neuron connections in the spinal cord At these connections (or in the dorsal roots) weak or interrupted sensations of pain from the heart coronary vessels or aorta supposedly are converted into stronger or continuous sensations of pain In the same regions of the cord at common synaptic junctions (or again possibly in the dorsal roots) similar impulses are amplified and in this form pass contralaterally and upward in the spinal cord to the thalamus There is a belief that in the thalamus and cortex these sensations may be amplified still further By virtue of this capacity of amplification impulses of pain reach consciousness vastly augmented and frequently beyond the possibility of control This phenomenon is assumed to operate for referred pain from all viscera but nowhere more conspicuously and dramatically than in that of anginal origin

C Residual Effects

In general direct pain within an organ splanchnic pain is weaker and less sharp than pain referred from an organ somatic pain This distinction be

tween deep "splanchnic pain" in a viscus and superficial 'somatic" peripheral pain was known to Ross, Head also differentiated "sharp, aching stabbing" referred pain from "dull, wearing" direct pain

Referred anginal pain is often much more intense and sharp than the sternal or retrosternal variety, and the pain may be wholly referred and the sternal region escape As referred pain subsides the affected region often undergoes a feeling of numbness or dullness Sometimes this effect is a tingling or a sharply localized thermal sensation, hot or cold The nerves that distribute referred pain may stay sensitive to pressure, or they may set up reverse and paradoxical attacks of pain, travelling toward the precordium Attacks of anginal pain have been provoked by pressure or thermal stimuli to extra cardiac surface areas on the left arm for example, and it would almost seem as if these areas become more readily responsive to the initiation of similar attacks after having experienced the first one The anginal pain that comes after chilling the skin belongs in this category

In addition to zones of hyperesthesia, trophic changes are known to appear and swellings in the breasts, even mastitis, in the arms and in fact in areas as far away as the lower limbs and testes The left arm, after an attack, may lose its motor power and atrophy of the muscles supplied by the ulnar nerve has *been noted Herpes zoster along the course of nerves that have carried anginal* pain is not altogether a rare occurrence

D Emotional Component

The emotional suffering seems to possess singular psychogenic traits that *are seldom seen in other types of agony, and the intensity of this emotional* picture overshadows that observed in nonanginal kinds of pain An intimation, therefore, may be in order that this inordinate psychic upheaval is produced in the higher centers through the intervention of some mechanism of amplification analogous to that described in connection with anginal pain

BIBLIOGRAPHY

1 Allbutt T C Diseases of the Arteries Including Angina Pectoris London Macmillan *1915*

2 Aronowitsch G D Über anginoide Anfalle bei Schmerzen im linken Brachialplexus Klin Wchnschr 1925 *4* 117

3 Ashkenaz D M *An experimental analysis of centripetal visceral pathways based upon* the viscero pannicular reflex Am J Physiol 1937 *120* 587

4 —— and Spiegel E The viscero pannicular reflex Am J Physiol 1935 *112* 573

5 Boas E P and Levy H *Extracardiac determinants of the site and radiation of pain in* angina pectoris with special reference to shoulder pain Am Heart J 1937 *14* 540

6 Boyer A De l angine de poitrine compliquant les nevralgies intercostales et brachiales gauches *Thesis Paris 1930 6 13*

7 Cushing H Peptic ulcers and the interbrain Surg Gynec & Obst 1932 *55* 1

8 Danielopolu D l angine de poitrine et l angine abdominale Paris Masson 1927

9 —— *J de Chirurgie 1938 51* 1

[18] —— AND DANULESCO V Transpozitie completa de viscere cu insuficienta mitrala aortica cronica Bull Asoc Brancovenesti 1916
[1] —— AND HRISTIDE Recherches sur la sensibilité cardiaque Possibilité d'améliorer l'angine de poitrine par la résection des racines postérieurs ou des nerfs spinaux. Comp rend Soc. de Biol 1923 88 271 Bull et mem Soc. Méd d Hôp de Paris 1923 47 69
[18] DAVIS L POLLOCK L J AND STONE T T Visceral pain Surg Gynec & Obst. 1932 55 418
[1] EDEIKEN J AND WOLFERTH C C Persistent pain in the shoulder region following myocardial infarction Am J M Sc. 1936 191 201
[1] EPPINGER H AND HOFER G Zur Pathogenese und Therapie der Angina pectoris Wien Klin Wchnschr 1923 36 334
[18] —— AND —— Die Therapie der Gegenwart Wien Klin Wchnschr 1923 64 169
[18] GOLDSCHEIDER A Behandlung der arteriosklerotischen Schmerzen Ztschr f Physikalische u Diät Therap 1910 13 3
[17] —— Über die operative Behandlung der Angina pectoris Klin Wchnschr 1925 4 2425
[18] —— Zur Frage der tiefen Druckempfindungen Klin Wchnschr 1925 4 9 9
[1] HEAD H On disturbances of sensation with special reference to the pain of visceral disease Brain 1893 16 1
[18] HEBERDEN W Some account of a disorder of the breast Med Trans Coll Phys London 1772 2 59
[1] HEINBECKER P Anatomic and physiologic criteria for surgical relief of cardiac pain J Thoracic Surg 1932 2 517
[18] HILTON J Rest and Pain A course of lectures on the influence of mechanical and physiological rest in the treatment of accidents and surgical diseases and the diagnostic value of pain 10th ed Edited by Jacobson W H London 190
[18] HURST A F (HERTZ) On the insensibility of the alimentary canal in health and disease Lancet 1911 1 10 1 1119 1187
[18] HOFER G Bericht u die Durchschneidung des Nervus Depressor bei der Angina pectoris (nach Eppinger H u Hofer G) Ztschr f Hals Nasen u Ohren 1923 6 68
[18] JENNER E Quoted by Osler W in Lectures on Angina Pectoris and Allied States New York D Appleton 1897
[18] LANGLEY J N The Autonomic Nervous System Cambridge W Heffer & Son 1921
[17] —— The sensory nerve fibres of the heart and aorta Lancet 1924 2 955
[18] —— AND ANDERSON H On reflex actions from sympathetic ganglia J Physiol 1894 16 410
[1] LEMAIRE Quoted by Danielopolu D
[1] LERICHE R La chirurgie de la douleur et ses resultats La Presse Médicale 1924 52 49 Ibid 192 36 561
[1] LIAN C L angine de poitrine Paris Masson 1932
[18] LIBMAN E Symposium Angina pectoris with special reference to coronary artery disease Bull New York Acad Med 1935 11 477
[18] LIVINGSTON W K The Clinical Aspects of Visceral Neurology Baltimore Chas C Thomas Co 193
[18] MACKENZIE J Some points bearing on the association of sensory disorders and visceral disease Brain 1893 16 321
[18] MARTYN S On the physiological meaning of inframammary pain Brit M J 1864 296 (Sept 10)
[18] MOORE R M MOORE R E AND SINGLETON A O JR Experiments on the chemical stimulation of pain endings associated with small blood vessels Am J Physiol 1934 107 594
MORLEY J Visceral pain Brit M J 193 12 0 (Dec 25)

[38] ODERMATT W Die Schmerzempfindlichkeit der Blutgefässe und die Gefässreflexe Beitr f Klin Chir 1922 *127* 1
[39] PARRY, C H An Inquiry into the Symptoms and Causes of the Syncope Commonly Called Angina Pectoris London Cadell & Davis 1799
[40] PENFIELD W The neurological mechanism of angina pectoris and its relation to surgical therapy Am J M Sc 1925 *170* 864
[41] PIKE F H On the difficulties encountered in the evolution of air breathing vertebrates Science 1924 *59* 402
[42] —— A further note on the difficulties encountered by land vertebrates in their development Science 1928 *68* 378
[43] —— An approach to the problem of pain fields with special reference to those associated with diseases of the nose and throat Laryngoscope 1928 *38* 219
[44] POLLOCK L J AND DAVIS L H Peripheral Nerve Injuries New York P B Hoeber 1933
[45] RANSON S W AND BILLINGSLEY P R The superior cervical sympathetic ganglion and the cervical portion of the sympathetic trunk J Comp Neurol 1918 *29* 313
[46] ROSS J On the segmental distribution of sensory disorders Brain 1888 *10* 333
[47] RYLE J A Visceral pain and referred pain Lancet 1926 *1* 895
[48] —— The clinical study of pain with special reference to the pains of visceral disease Brit M J 1928 *1* 537
[49] SCHRAGER V L AND IVY A C Symptoms produced by distention of the gall bladder and biliary ducts A clinical and experimental study Surg Gynec & Obst 1928 *47*
[50] SPIEGEL E A Über das Wesen des Bauchschmerzes und eine Begleiterscheinungen Wien med Wchnschr 1927 *77* 379
[51] —— Experimentelle Neurologie Berlin S Karger 1928
[52] —— Visceral and vascular pain Proc Staff Meet Mayo Clin 1930 *5* 213
[53] —— AND HASHIMOTO S Über die Schmerzleitung aus dem cardioaortalen System in Beziehung zu den Spinalganglion und den Ruckenmarksbahnen Ztschr f d ges exp Med 1930 *71* 408
[54] —— AND WASSERMANN S Experimentelle Studien uber die Entstehung des Aortenschmerzes und seine Leitung zum Zentralnervensystem Ztschr f d ges exp Med 1926 *52* 180
[55] STOHR P JR Mikroskopische Anatomie des vegetativen Nervensystems Berlin J Springer 1928
Bemerkungen zur Gefassinnervation Zentralbl f Chir 1934 *61* 2
[56] SUTTON D C AND LUETH H C Pain Arch Int Med 1930 *45* 827
[57] WEISS S AND DAVIS D The significance of the afferent impulses from the skin in the mechanism of visceral pain Skin infiltration as a useful therapeutic measure Am J M Sc 1928 *176* 517
[58] WENCKEBACH K Angina pectoris and the possibilities of its surgical relief Brit M J 1921 *1* 809
[59] WHITE J C The Autonomic Nervous System New York Macmillan 1935
[60] —— Chapters 5 and 15 in Diseases of the Coronary Arteries and Cardiac Pain Levy R L New York Macmillan 1936

CHAPTER XII

The Simulations of Anginal Pain, Angina Pectoris, and Acute Myocardial Infarction

THE SIMULATIONS of anginal pain are not to be confused with its abnormal projections (p 31) The latter represent examples of anginal pain with uncommon references whereas in simulations the pain that originates in non cardiac organs or other structures is evinced in the heart and in adjacent regions These simulations from a practical point of view are best grouped with regard for their regional locality Clinically other types of heart pain produced by nonanginous cardiovascular disease or by general toxic agents fall into other groups

I The Simulation of Anginal Pain in the Sternum or in the Region of the Sternum

Since anginal pain as we have defined it is so frequently and customarily localized in the sternal region or deep beneath it in the chest there is the danger of overlooking non cardiac causes of pain in these regions These causes are numerous The skin overlying the sternum the subcutaneous tissues the sternum itself may be the seat of infections or the sternal articulations are attacked by arthritic changes after an allergic or infectious (toxic) process Rheumatism of the articulations of the breastbone including the claviculosternal is rare but it does occur also involvement from gonorrhea or in gout Pathological alterations of any of the contents of the anterior mediastinal space may localize pain in the region of the sternum the lymphatic glands and loose areolar tissue the blood vessels and nerves Gastralgia from hyperchlorhydria or obstructive conditions of the lower esophagus diseases of the stomach or of the dome of the diaphragm will induce pain in or directly beneath the sternum also traumatic injuries inflammations or neoplasms of the viscera in the other mediastinal compartments Pressure of tumors aneurisms sacculations of fluid in the pericardial or pleural spaces is able to register pain within or close to the boundries of the sternum A curious and rather ill-defined type of pain resembling in some respects the anginal is that described by Posselt[24] intermittent claudication developed it is alleged in the pulmonary vessels The nearer the lesion is to the sternum the better defined will be the sternal localization of pain and the greater the possibility therefore of confusion with anginal sternalgia

II Into the Left Anterior Chest or Pectoral Region

As far as the thorax is concerned, anginal pain and its reference are practically always confined to the left anterior wall It is much less common to have the corresponding left posterior wall or the posterior axilla participate Only the non cardiac conditions, therefore, with pain and reference in this anterior region are germane to this discussion

Diseases of the superficial tissues are painful also of the breasts, mastitis, hematoma, unusual hypertrophy with pain from its dragging weight Sometimes the pain associated with neurofibromata or generalized adiposity is localized here Myalgias of the pectoral muscles or infections (abscess), neuralgias along the anterior thoracic nerves to the major and minor pectoral muscles (C 5, 6 7, 8 and Th 1), radicular pains manifested occasionally with a Herpes Zoster and confined to the anterior chest, offer difficulties in differential diagnosis Local pain accompanies osteomyelitis, periostitis neoplasms or nutritional or endocrinal disturbances of the bony parts of the thorax, blood dyscrasias, multiple myeloma, and metabolic disorders belong here There are also disorders of the left chest with contralateral or bilateral pain

III Into the Left Upper Extremity the Shoulder and the Rest of the Limb

The left shoulder is not commonly part of the anginal radiation that begins in the precordium and ends in the fingers but it may be either by itself or together with radiation well into the hand, the sole locality of anginal pain (Edeiken and Wolferth,[10] Libman,[19] and Boas and Levy [6] etc) As a consequence, a number of nonanginal types of pain in the shoulder require differentiation from the anginal pain in this territory Inflammations etc of the overlying tissues cervical arthritis and subacromial bursitis, belong in this group Arthritic alterations in the shoulder girdle are painful, also neoplasms, etc in and about the bones of the joint The deltoid (C 5 6) and trapezius (C 3, 4) muscles very occasionally are touched by anginal pain through the intervention of afferent somatic or visceral fibers (Fig 54) or possibly through the vagus as it connects with the upper cervical nerves More often these muscles are the locations of painful local conditions or of nonanginal references i e from the diaphragm by way of the phrenic nerve into the 4th occasionally into the 3rd and 5th cervical nerves Non anginal pain in the biceps muscle has a similar general significance in relation to anginal pain

The characteristic spread of anginal pain covers the small territory of the left anterior axilla supplied by the second thoracic nerve and the inner aspect of the left upper arm and forearm down to and including the ventral aspect of the little finger supplied by the second and first thoracic nerves forming an ulnar distribution In contrast pain in the left arm from non cardiac causes is practically always more extensive in area and overlaps zones supplied by the

musculo-cutaneous nerve (C 5 6 and in many cases 4) or the radial musculo-cutaneous nerve (C 5, 6 7 8, Th 1) or the median nerve (C 5, 6 7 8 Th 1) as well as the ulnar nerve (C 8 Th 1 and in many cases C 7) Moreover the pain is of the diffuse and not of the radicular type

Neuritis of the left cervical or brachial plexuses is extremely painful It follows fractures or dislocations of the neck or shoulder or results from pressure to the plexus from tumors aneurisms in the neck or vertebral caries The neuritis after infections (influenza) from taking cold or from poisons (toxic agents) is quite inten e The spread of this pain varies with the extent of the involvement of the plexus Lesions that attack the 4th 5th 6th and 7th and 8th cervical nerves produce pain in the shoulder in the axilla and along the back of the arm sometimes into the forearm and the muscles supplied by this innervation sometimes develop paralysis (deltoid biceps coracobrachialis and supinator muscles) The neuritis that strikes the lowest cervical nerves includ ing the 1st thoracic nerve may move across the clavicular reg on and along the front of the arm and into the hand and fingers and the muscles of this innervation also suffer paralysis

The neuritis of the lower cervical nerves is apt to encroach upon the left cervical sympathetic trunk producing left oculo pupillary signs Horner s syn drome i e contraction of the pupil and inability to dilate fully narrowing of the palpebral aperture and slight retraction of the eyeball also slight pallor of the left face and neck marked dryness of the nostril and mouth and a de crease of the sweat secretion of the neck arm and chest flushing and per pira tion are subnormal An unusual form of neuritis associated with injury to cervical sympathetic nerves was described by Klumpke and is sometimes called Klumpke s palsy

Brachial neuritis is a common disorder very painful occasionally very ab rupt in its onset The arm is kept immobile because of the intense pain and paresthesias are frequent and troublesome Muscles supplied by the affected nerves are likely to show paralysis and later on atrophy trophic skin changes are common The condition lasts several weeks or months then subsides slowly leaving residual weakness for several weeks *Brachial* as well as cervical neu ritis flares up violently and lingers in gout diabetes anemias and leukemias and the neuritis from alcohol metallic and other poisons and from vitamin deficiency is common knowledge

The presence of a cervical rib is often not always attended by homolateral neuralgia Distribution of pain etc varies with the portion of the cervical or brachial plexus compressed From prolonged pressure the muscles of the limb undergo atrophy generally those of the fingers and the hand below the wrist a sign of diffu e not radicular nerve involvement The muscles show R D The sensory loss in the cutaneous area again varies with the parts of the plexus damaged touch is not greatly disturbed At some stage neuritis from a cervi

cal rib may be constant and unrelieved More often it is intermittent and aggravated by exertion or in unfavorable posture of the body, and relieved when the pressure of the rib against soft tissues is lifted as when placing the hand behind the head In most cases an x ray will reveal the rib and fix the diagnosis but in some cases a negative x ray gives no intimation of the existence *of a ligamentous band pressing upon the nerves at a spot corresponding to a* supernumerary rib

Although syringomyelia is characterized primarily by a loss of pain sensation together with perception of temperature, this disease may be painful and in the case of cervical cord affections, emit darting neuritic pains down the arm A neuritis of left cervical distribution may lead to confusion with referred anginal neuralgia Generally speaking, however, in its developed form syringomyelia will not be overlooked or mistaken for anginal pain First of all, there is selective crippling of the sensory fibers that carry sensations of temperature and pain, those for tactile sensation remaining intact This disturbance, named by Charcot dissociate anesthesia is a striking characteristic and no less striking is the frequency with which this dissociate phenomenon remains unknown to the patient until revealed to him by the physician Other characteristic aspects of the disease are the trophic changes in the skin, muscles joints and skeletal parts, and gradual muscular atrophy and paralysis

Variations of symptoms depend upon the extent to which the spinal cord is involved, leading to spastic paraplegia to derangements in tactile sensations *with pain etc The physical signs and symptoms are bilateral* but not necessarily symmetrical

Lian[18] and his pupil Boyer,[6] described a form of very severe left brachial and intercostal neuralgia in which reference of pain into the precordium is prominent This pain in localization, character and associated signs simulates anginal pain Not only this but all left sided brachio intercostal pains have a certain resemblance to the anginal variety of radiation *The latter however, is* usually radicular with patchy zones of dermatomic reference the former, as a rule, diffuse and irregular This point and others described above, help in accurate differentiation

Radicular or diffuse unilateral pain with limitation to a portion of the left arm is associated with affections of the vertebra spondylitis, for example of the upper thoracic or cervical region Pain of this origin is prone to grow worse with uncontrolled movements of the body during sleep, exertion or unfavorable postures of the body intensify the pain and rest and measures of immobilization bring relief Affections of the spinal cord may or may not cause neuritic pain, moreover, lesions of the cord result in bilateral signs not always symmetrical, with paralysis of the parts above and spastic signs of the parts below the level of the lesion

IV Into the Left Side of the Face, Neck Head

The face and neck usually escape anginal pain, though it is known to get into these regions Much more frequently pain in these parts is due to other causes

There are special points of interest about the pain which enters the head and the cerebral structures In such instances one must make certain that the pain in these distributions is not of anginal origin because as we have previously observed (Chapter XI) it is possible for the sensory component of the fifth nerve and the tenth nerve to carry anginal pain and possibly the sensory portions of the seventh and ninth nerves act in a similar manner

V Thoracic Conditions that Simulate Anginal Pain

Lung diseases pleurisy herniations at the diaphragm and other diaphragmatic disorders (including subdiaphragmatic conditions) are capable of producing chest pain in or near the heart The intermittent claudication of pulmonary vessels (Fosselt) has been mentioned Thrombosis of large veins in the thoracic cavity seen in rheumatic cardiovascular disease or after injury or with arteriovenous anastomosis or in diseases of the blood or with deep phlebitis from any infection (including the migrating type) are painful If the lesion is left sided sinistral radiation into the cervical or brachial plexus may occur Anginal pain may appear with pulmonary embolization and infarction the embolus may have a cardiac or peripheral venous origin

VI Cardiovascular Conditions with Simulated Anginal Pain

Lesions of the pericardium in general and especially those close to the aorta and other large vessels may cause pain that resembles the anginal variety As a rule however painful pericarditis is not mistaken for anginal pain The fresh pericarditis with heart muscle infarction produces pain it is localized aggravated by movements of the chest and by pleural complications The pathway of pericardial pain is by way of the phrenic nerves into the fourth cervical dorsal root and along the fourth cervical nerve into the shoulder region (Coffey and Brown and Humber* have described an anastomosis between the phrenic nerve and the superior sympathetic cardiac nerve)

Distention of the aorta in hypertension is usually painless Dilatation of the aortic ring a feature in the dilated flabby heart of marked anemia is occasionally accompanied by cardiac pain The pain of aortic regurgitation manifested in luetic aortitis with its obstructive encroachment on the coronary orifices does not belong in this category of heart pain it has already been described under anginal pain Aneurism of the aorta produces pressure pain and not anginal pain it has been known however to produce anginal pain and even the rest of the anginal syndrome (Osler[21]) Coiled and elongated arteriosclerotic aortas are not painful A dissecting aortic aneurism may be ex

tremely painful and intense pain is associated with sudden blocking of the large tributaries of the aorta as from embolization

Rheumatic aortic disease and arteriosclerotic alterations especially when accompanied by stenosis of the valve are painful in some cases Pain occurs in advanced arteriosclerotic alteration of the aortic valve Rheumatic disease that attacks the mitral valve, the stenotic variety, produces pain, somewhat more frequently in children (Schwartz[6]) The pain that arises in disease of the blood vessels in the chest has already been mentioned (p 38) Precordial pain, even radiating into the arm, is known to appear with sudden or severe derangement of the rhythm of the heart, particularly of the paroxysmal variety, i e, auricular or ventricular tachycardia paroxysmal auricular flutter, paroxysmal auricular fibrillation, and some forms of heart block also belong here The pain in many of these instances is due to acute coronary insufficiency associated with some degree of ischemia of heart muscle Pain under these circumstances is truly anginal in character

VII Simulation from Abdominal and Pelvic Conditions

We have already suggested that pain and the rest of the anginal syndrome will stem from a physiologic mass action of the entire autonomic system and that the different constellations of signs and symptoms vary with the specific pathways called into action

The same mechanism functions in the case of abdominal or pelvic organs that produce pain Most diseases of these viscera develop no "heart" pain, but this kind of pain, however is capable of reaching the cardiac territory and of simulating anginal pain It is either a mild, more benign type, comparable to interval pain or intense and paroxysmal The latter together with manifestation of shock anxiety, etc, are hardly distinguishable from the state attendant upon acute myocardial infarction with or without coronary occlusion The angina pectoris or acute myocardial infarction masquerade of abdominal disease therefore is responsible for tragic errors in surgical judgment Acute generalized postoperative peritonitis simulating acute coronary occlusion is a striking case in point (Averbuck[4])

Acute gall bladder disease (cholecystitis empyema) acute pancreatitis, sudden perforation of the stomach duodenum or intestine are explosive conditions characterized by pain and often with references of pain and by general manifestations again suggesting a mass excitation of the entire autonomic system This is analogous to the state of affairs that prevails in an attack of angina pectoris and we could, therefore with some relevancy speak of "angina pectoris" of the gall bladder or of the pancreas Intense colic from bowel obstruction or from mechanical obstruction to any hollow structure ureter bile duct, etc, from extensive infarction of an organ or from thrombosis in large abdominal or thoracic vessels (including the pulmonary) or dissecting aneurism of the aorta, all these induce pain and associated features closely simulating the

intense attack of acute myocardial infarction with or without acute coronary thrombosis Although of rare occurrence the pelvic organs male or female engender pain that finds its way to the cardiac region the reverse of this has been described in Chapter XI Abdominal viscera act in a similar way the organs closest to the diaphragm causing the most pronounced effects For example in no other condition is angina pectoris or acute myocardial infarction more closely simulated than in esophageal herniation Upper abdominal organ possess a double and full innervation (sympathetic and parasympathetic) and perhaps also a more diffusely developed system of visceral afferent fibers Organs lower in the celomic cavity are not as well developed in this respect, and this may account for their comparative immunity as sources of explosive episodes

Surgical conditions of the abdomen and pelvis do not as a rule offer any insurmountable difficulty in differential diagnosis from angina pectoris or acute myocardial infarction but there are unfortunately enough exceptions when a differential diagnosis is almost impossible and the reason for this to some extent we have tried to clarify elsewhere in this text (Chapter XI) We see no point in connection with this problem to detail extensively the signs and symptoms of the surgical conditions that attack the abdomen and pelvis Although these are well known even experienced physicians well grounded in these details encounter cases that defy accurate diagnosis

VIII More General Causes that Simulate Anginal Pain

These form a rather large but ill-defined group

A Toxic Agents and States

Of these poisons like lead and arsenic etc and the abuse of tobacco are held under special suspicion These substances exert a general noxious influence on the nervous system deranging vegetative centers or peripheral nerves or perhaps set up allergic changes or some degree of chemical alteration of which pain in the heart and reference is one feature Nutritional deficiency tates probably belong here also

Tobacco To speak of the simulation of anginal pain from tobacco presupposes that tobacco can cause anginal pain The guilt of this weed however, as a cause of anginal pain is not entirely clear Allbutt believed smoking causes violent angina *Huchard*[13] *described* several clinical forms of tobacco angina and emphasized the effect of nicotine especially in connection with the production of arteriosclerosis on the other hand Brooks[f] from his experience refused to inculpate tobacco The literature contains many statements pro and con To name but a few Fiessinger[t] published cases with a precipitating and lethal effect of tobacco hard to deny and Moshcowitz[m] reported several cases with symptoms closely simulating anginal pain

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autonomic nervous centers On the other hand these poisons have a peripheral effect and cardiac pain may be therefore a consequence of an induced neuritis for example or perhaps even of a toxic action on heart muscle

B Drugs

Adrenalin is known to induce pain in the heart and insulin has precipitated paroxysms practically identical with those of angina pectoris this occurs more frequently in anginal sufferers than in normal subjects There is some times a generally accepted notion that caffeine and strong tea also may produce pain in the heart While it is conceded that these substances bring some degree of cardiac distress from cardiac overactivity or mild arrhythmia they have no great practical significance as instigators of heart pain

C States of Asphyxia

This has been alluded to elsewhere (Chapter X) Conditions of low oxygen artificially produced as in testing the endurance of aviators or in very high altitudes provoke pain in the heart Asphyxiating gases may also cause cardiac pain

D Anemias and Other Blood Conditions

The heart exhibits pain not always to be sure in impoverished states or disorders of the blood forming tissues Callavardin[11] reported two striking instances of pronounced precordial pain with radiation into the left arm due to hemorrhoidal loss of blood and sudden severe loss of blood from gastric ulcer leads to acute coronary insufficiency and anginal pain (Scherf [23] Master et al [20] Buchner [8] Aschenbrenner[3]) Anemias more especially pernicious anemia have neuritic features and these in the left arm or chest may simulate anginal pain

E Endocrine Disorders

Heart pain is associated with endocrine disorders and in menopause precordial pain may appear Sometimes it is associated *with hypochromic anemia* at this stage of life or without anemias flushing hot and cold sensation emotional changes and neuritic pain in the limbs are frequent

Myxedema Meissner [1] Zondek [25] Fahr [11] reported cardiac enlargement (dilatation) in myxedema that *receded on thyroid therapy* heart pain was not a feature In view of this the case reported by Laubry Mussio Fournier and Walser[17] and two cases published by Abrami Bruk and Heitz[1] have unusual interest Thyroid therapy stopped *the paroxysm* and helped the myxedema in the cases of Abrami et al the therapy aggravated a hypertensive state

Graves disease Cardiac pain is sometimes observed in this condition with its profound autonomic derangement and cardiac hyperactivity The pain

It is common experience to observe heart pain or distress from smoking in a certain number of healthy and perhaps more often in cardiac subjects The older view held *nicotine responsible, but this has no established foundation* In statistical studies, to mention but one publication, White and Sharber[7] from an analysis of 750 cases of anginal pain found no more smokers than in a control group of 750

There are of course, individual differences in sensitivity to tobacco For some a large amount of tobacco is innocuous for others with marked sensitivity a small quantity is injurious as from an occasional short inhalation of tobacco smoke or absorption of tobacco protein through the mucous membranes of the mouth These short exposures to tobacco are known to induce pain in the heart or aggravate an already existing anginal state More recent investigations point to a relationship between tobacco and the cardiovascular system

Harkavy[14] believes the incidence of sensitivity to tobacco protein (he is careful to make it clear that he is not speaking of nicotine) is high in individuals who have vascular disease For example, of 140 subjects with thrombo angiitis obliterans *70 per cent gave a positive skin reaction to various tobaccos* tested and of these positive reactors, one half had reagins (antibodies) to tobacco in the blood serum About one tenth of the number of the 70 per cent possessed a general constitutional allergy to many proteins This would signify *that of the total 140 cases with thrombo angiitis obliterans 60 per cent were* essentially sensitive to tobacco but were free of every other type of protein sensitivity In contrast were some 400 unselected normal smokers as a control group of these only 10 per cent were positive to tobacco alone out of a total of 38 per cent who reacted not only to tobacco but also to the proteins of timothy hay ragweed and horse dander in various combinations

Similar observations on coronary artery disease disclosed results of special significance with respect to angina pectoris Testing 100 subjects with coronary artery disease Harkavy uncovered about 40 per cent that were sensitive to tobacco as well as to some of the proteins listed above Of these 33 per cent had personal or family histories of allergy This contrasted with an incidence of 10 per cent of constitutional allergy in the thrombo angiitis obliterans group Of the 40 per cent reacting to tobacco two thirds had reagins to tobacco in their circulation Finally a point of some clinical import the majority of these hypersensitive coronary artery disease subjects fell into an age group averaging 45 years or younger

These studies appear to confirm the clinical impression that the cardiovascular system is peculiarly vulnerable to the ravages of tobacco and seems to act within certain limits as an allergic shock organ

Lead arsenic other metals These have the common property of acting on the vegetative centers It is, therefore conceivable although no proof is at hand, that these poisons produce cardiac pain as part of the reaction of the

dividuals with so called circulatory neurasthenia soldier's heart,' belong here

All these individuals may be regarded as belonging to a hypersensitive group (Chapter XIV) It is well to appreciate however that angina pectoris and acute myocardial infarction show no tendency to spare them as a class in deed large numbers are victims During the throes of a severe paroxysm espe cially if acute coronary occlusion has occurred there is seldom any doubt about the true nature of the malady but after recovery the patient may com plain of precordial pain and radiation or of apprehensions that tax the diag nostic skill of the attending physician Are these subjective signs without any organic basis or are they the attestations of recurrent occlusions in small coronary twigs or of episodes of acute coronary insufficiency? The answer is that one or all may occur but the important fact will remain that it is wiser and safer to look upon these complaints as not imaginary in view of the past history of the patient and to temper the prognosis against the hypersensitive background of this type of individual One can never wholly disregard the anginal factor in a person who has once had a genuine paroxysm

There is still another group of individuals who over many years have suf fered with pain that seems to arise from various viscera In many instances the pain is so intense and so well localized that surgical treatment is instituted These individuals are apt to suffer the removal of appendix gall bladder pelvic organs only to continue to have pain in their remaining organs often the heart with radiation into corresponding dermatomes Apparently these pains have no organic basis and are induced by psychogenic states for exam ple by reaction to fear to subconscious causes or to conditioning mechanisms Many of these subjects are conversion hysterics who express the conversion by cardiovascular features with precordial pain and radiation a prominent manifestation

BIBLIOGRAPHY

[1] ABRAMI P BRULÉ M AND HEITZ M Complications of two cases of angina pectoris with myxedema hypertension aggravated by thyroid therapy Bull et mém Soc méd d Hôp de Paris 1925 49 412

[2] ALLBUTT T C Diseases of the Arteries Including Angina Pectoris London Macmillan 1915

ASCHENBRENNER A Mangelnutung und Anoxie des Herzmuskel Ztschr f klin Med 1935 127 160

AVERBUCK S H Acute generalized postoperative peritonitis simulating coronary artery thrombosis J Mt Sinai Hosp 1942 8 335

[4] BOAS E P AND LEVY H Extracardiac determinants of the site and radiation of pain in angina pectoris with special reference to shoulder pain Am Heart J 1937 14 540

BOYER A De l angine de poitrine compliquant les nevralgies intercostales et brachiales gauches Thesis Paris 1930 6 13

BROOKS H Angina Pectoris New York Harper & Brothers 1939

may require separation from the anginal type particularly in subjects with auricular fibrillation or other signs which denote myocardial alteration

F Miscellaneous

Laubry[18] had a remarkable experience of witnessing intense precordial pain with radiations into both arms, shock, etc, pointing to angina pectoris in a man of 60, a smoker, who, two days later, proved to have epidemic encephalitis

Biliary duct disease also has been described with the occurrence of anginal pain, and Osler[23] wrote of the association of anginal pain with migraine attacks and with Raynaud's disease Much has been published on the connection between angio spastic states of blood vessels in general and the coronary vessels (p 281)

Pain in the heart is not a rare occurrence in subjects with gout and diabetes mellitus Coronary artery disease is, of course common in individuals who have these afflictions The matter of incidence in similar age groups may be relevant or it may be that the metabolic disease is fertile soil for the development of occlusive manifestations in the coronaries and other vessels These metabolic disorders however, are alleged to induce non anginal cardiac pain, that is to say, in the absence of involvement of the coronary circulation Libman[19] mentions a case in point

In diabetes mellitus pain in the precordial region, especially with radiation into the cervico brachial plexus or into lower intercostal nerves suggests some form of neuritis The neuritic pain, as we have indicated is able to "flow" toward the heart region and so simulate either anginal pain or even the entire syndrome of angina pectoris An interesting corollary is the severe precordial pain with radiation and other features of angina pectoris precipitated by the administration of insulin

G Emotional States

Many emotional states ranging from intense anger, grief, fear mental distress to mild upsets of worry or anxiety produce pain that is felt in the heart This pain is nonanginous unless the heart coronary vessels or aorta are actually implicated (p 194)

There are many kinds of nonanginous pain in the heart or in the chest region of the heart variously termed heart pang' heartache' etc They range from mild almost gentle discomforts or paresthesias to sharp and severe or dull and throbbing manifestations Their duration is, as a rule brief The subjects are usually high strung neurotic individuals heart conscious and nervously apprehensive often sensitive to any discomfort and generally tired and fatigued They have nervous heart trouble or pain and are very apt to be on the defensive regarding the validity of their symptoms or complaints In

SECTION FIVE

Concept and Mechanism of Anginal Pain

CHAPTER XIII

Physiologic Aspects of Pain

1 General Considerations

PAIN has general biologic and more specifically physiologic significance Biologically it is allied to other sensory phenomena and seems to act within certain limits as a premonitory warning and as a protective mechanism The registration of pain in consciousness i e the recognition of pain probably belongs in the realm of psychology the initiation and transmission in the realm of physiology

From the physiologic point of view pain depends on two factors the nature of the stimulus and the function of the nervous apparatus which receives and transmits it and registers the effect The outer integument of the body is richly endowed with many nerve endings from which nerve fibers go to the cerebrospinal system and along these fibers a variety of sensations are conveyed There are nerve endings for picking up tactile and thermal sensations and special nerve endings with arborization arrangements for pain Moreover, certain zones in the skin are unusually hypersensitive to pain the cornea for example the tympanic membrane the nail beds the junctions of skin and mucous membrane at the mouth and anus The finger tips lips and genitalia and anus are richly supplied with all forms of nerve endings The cornea, tympanum and dental pulp possess pain receptors only

The muscles covered and protected by the skin or outer envelope of the body are not required to appreciate or discern thermal or tactile sensations but they can produce pain after extreme or prolonged contractions or marked stretching Muscles become painful when their usual range of activity is exceeded and cramps in the muscles are everyday occurrences Muscular activity is observed also in hollow organs of the body i e bile passages gastrointestinal tract genitourinary tract arteries the lining or inner coat of these structures contrasted with the skin is insensitive to pain The outer coat or serous layer is likewise insensitive yet the organs it encases readily become the site of pain when the muscular layers are provoked into exaggerated or prolonged contractions for example in overcoming an obstruction in a lumen Muscular contractions beyond a certain point or threshold in other words an increased tension of the muscle fibers is announced as pain

Solid organs like the brain the liver the spleen the kidneys are insensitive to stimuli that readily produce pain in the skin Countless incidents are on

[8] BUCHNER, F Die Koronarinsuffizienz Dresden u Leipzig Theodor Steinkopff 1939
[9] COFFEY, W B, BROWN, P K, and HUMBER, J D Angina Pectoris The Anatomy Physiology and Surgical Treatment New Orleans A J Dickerson 1927
[10] EDEIKEN, J, AND WOLFERTH, C C Persistent pain in shoulder region following myocardial infarction Am J M Sc 1936 *191* 201
[11] FAHR, G Myxedema heart J A M A 1925 *84* 345
[12] FIESSINGER, C L'angine de poitrine tabagique Rev gén d clin et d ther 1913 *27* 690
L angine de poitrine tabagique Ibid 1919 *33* 169, Le mort par le tabac dans l angine de poitrine Ibid 1923 *37* 827
[13] GALLAVARDIN, L L angine de poitrine d effort dans les états anemiques post hemorrhagiques Pratique médicale française 1925 *6* 10
[14] HARKAVY, J Personal communication
[15] HUCHARD, H Maladies du coeur et des vaisseaux arteriosclerose aortites cardiopathies arterielles angine de poitrine Paris O Doin 1889
[16] LAUBRY, C Syndrome angineux et encephalite epidemique Bull et mém Soc méd d Hop de Paris 1924 *48* 1588
[17] —— MUSSIO FOURNIER AND WALSER J Syndrome angineux par insufisance thyroidienne Bull et mém soc méd d Hop de Paris 1924 *48* 1592
[18] LIAN, C L angine de poitrine Paris Masson 1932
De l angine de poitrine compliquant les nevralgies thoracobrachiales gauches Rev belge soc méd 1931 *3* 354
[19] LIBMAN, E Symposium Angina pectoris with special reference to coronary artery disease Bull N Y Acad Med 1935 *11* 427
[20] MASTER, A M, DACK, S, GRISHMAN, A, FIELD, L F, AND HORN, H Acute coronary insufficiency an entity Shock hemorrhage and pulmonary embolism as factors in its production J Mt Sinai Hosp 1947 *14* 8
[21] MEISSNER, R Münch med Wchnschr 1920 *67* 1316 Ibid 1921 *68* 488
[22] MOSCHCOWITZ, E Tobacco angina pectoris J A M A 1928 *90* 733
[23] OSLER, W Lectures on Angina Pectoris and Allied States New York D Appleton & Co 1897
[24] POSSELT, A *Die Klinische Diagnose der Pulmonalarterienskler*ose Münch med Wchnschr 1908 *55* 1625
[25] SCHERF, D Ein Fall von Angina pectoris Ztschr f Klin Med 1932 *120* 415
[26] SCHWARTZ, S P Paroxysmal cardiac pain The syndrome in young adults with rheumatic valvular heart disease Am Heart J 1927 *2* 497
[27] WHITE, P D AND SHARBER, T Tobacco alcohol and angina pectoris J A M A 1934 *102* 655
[28] ZONDEK, H Das Myxodemherz Münch med Wchnschr 1918 *65* 1180

in cutting this nerve pathway Elsewhere we have commented upon these views (Chapter XVI)

States of intravascular pressure within the aorta and the special bearing this has upon the aortic nerve endings (perhaps including also the nerve supply and action of the carotid sinus [Koch[13] Hering[15] Heymans et al[14]]) are invoked as responsible mechanical agents for the provocation of anginal pain On this basis with the vagus and the depressor nerve in constant touch with the heart and with their participation in the regulation of pulse rate and systemic blood pressure the aorta is looked upon as a kind of tambour for the announcement of effects within and for the initiation of important regulatory reflexes not only pain By bringing into prompt action a reflex fall in systemic blood pressure this trigger ready action of this part of the aorta renders it possible to ward off distention in this vessel and in the heart also The individual is thus in possession of a wider margin of safety and not only is pain warded off but more important sudden and overwhelming cardiac inhibition The action of the vagus and depressor nerve have been aptly called the safety valve of aortic and cardiac distention

The aortic theory has received the brunt of many onslaughts and a seeming telling blow is the absence of a depressor nerve in man (Chapter IX) This blow however is not as devastating as one might believe The existence of sensory fibers in the vagus is not questioned and these may be capable of carrying pain impulses from the aorta Moreover, there are sympathetic fibers from this region (aorta) that possibly function in a similar way and indeed some anatomists find that the equivalent of the depressor nerve may consist of sympathetic strands

B CORONARY ORIGIN

A second concept has been advanced that the coronary vessels of the heart are the primary seat of anginal pain Here again there are chemical and mechanical stimuli at work The chemical are either in the nature of solutions or substances acetylcholine or sympathin (adrenin like) etc liberated during the transmission of impulses to the nerve endings or chemical substances elaborated during the metabolism of heart muscle the proclivity of these latter substances to produce pain is regulated by the amount and character of the blood supply to the heart muscle

Mechanical stimulation also accounts for pain that arises in the coronary vessels These vessels are very prone to suffer temporary or prolonged occlusion In the former instance pain attends the transient block or constriction in the latter pain is an accompaniment of the first hours that ensue It has therefore been argued that pain follows from the initial spasm present in both instances and that the block itself is not a responsible agent This is not the place to dilate on this subject but data exist to indicate that the mechanical

record of sharp and deep wounds or lacerations to these organs in which no pain was experienced The coverings of these organs, however, are responsive to pain producing stimuli, such as injuries, inflammations stretchings, pressure, etc As a result, headache from meningeal irritation is common, pain from hepatic, splenic or renal capsular involvement is not rare It seems that in these solid organs, the likelihood for the occurrence of pain is in direct relation to the linear distance that separates the lesion in the organ from the envelope that encases it The heart and its envelope, the pericardium, are no exception

While pain in the foregoing conditions is caused by a variety of stimuli, in cardiac, coronary or aortic pain the stimuli are primarily mechanical or chemical

II Sites of Origin of Cardiovascular (Anginal) Pain

The victim of anginal pain, and for that matter of any type of heart pain, is unable to localize accurately in what structure his pain originates It is sometimes stated that any pain that starts in the aorta or coronary vessels or heart muscle possesses some distinguishing traits in each instance This view is maintained by some but most agree that differentiation on this basis is not possible Be this as it may, it is, nevertheless, of practical value to consider these three anatomic structures as the chief sites of the origin of anginal pain

A Aortic Origin

With respect to the aorta the theory has long been held that anginal pain and the entire anginal syndrome is produced in the first or ascending portion (As a matter of interest Heberden's[13] description of angina pectoris has been interpreted as of aortic origin) This theory presupposes the mechanical or chemical irritation of sensory nerve endings in this proximal portion of the aorta which undergoes spasm and leads to the most frequent variety of anginal pain, substernal The occurrence of spasm or constriction is supposedly facilitated by alterations in the vessel wall or of its nutrient channels According to Allbutt[2–4] and to Wenckebach [30] the spasm follows mechanical and chemical irritation or upon intravascular alterations of tension, and sensory impulses from the aorta travel along the so called depressor nerve, a vagal structure Vaquez [9] also was a strong proponent of the aortic genesis of anginal pain and angina pectoris, and Allbutt and Wenckebach were the chief advocates of the importance of the depressor nerve Allbutt wrote that this nerve became hypersensitive worried," in angina pectoris that it was stung by anginal pain to act upon the heart often decrescent and in this way caused cardiac inhibition and death

Wenckebach not only upheld the aortic genesis and the role of the depressor nerve but, with others in Vienna maintained that the relief of anginal pain lay

neutralized or enhanced by (b) an adequacy or deficiency of the circulation to the muscle affected Ischemia proves to be a common underlying factor in many situations Thus anginal pain is frequent in disease of the heart muscle or of its irrigating channels or of the proximal part of the aorta and in any of these circumstances ischemia of heart muscle may be an associated factor A pecial form of coronary artery disease s attended by a high incidence of angi nal pain namely luetic disease of the orifices of these vessels Here the req uisite blood supply to the heart muscle is diminished and ischemia obviou ly is not an unanticipated consequence Anginal pain is not at all rare in cardiac or even normal individuals suddenly subjected to low oxygen tension as in attaining great mountain heights (Monge[1 ""]) or working at industrial proj ects at low barometric pressure Anginal pain is encountered in severe anemia in poisonings which lower the oxygen capacity of the blood, and after severe exercise individuals who have had cardiac pain may develop anginal pain with characteristic electrocardiographic signs or electrocardiographic signs may occur without the pain (Katz[17]) Tennant and Wiggers[5] believe that anginal pain is produced by the periodic stretching of damaged heart muscle, similar to the stretching of muscle elsewhere in the body i e gall bladder intestine etc

Studies of the chemistry of ischemia have uncovered new and significant data Lewis Pickering and Rothschild[19] found special metabolites formed dur ing the contraction of skeletal muscle these products stimulated the pain nerve endings They labelled these chemical products P factor The same products or I factor elaborated at a much lower rate were found in muscles at rest This was established by Perlow Markle and Katz [1] The concentration of these metabolites was greatly hastened in the case of heart muscle when the organ was compelled to contract in the face of difficulties i e high aortic pressure or when already damaged as in marked dilatation of its chambers and from the ligaturing of a coronary vessel the related muscle segment was shown to develop excessive quantities of lactic acid with depletion of glycogen On all these grounds an ischemia of heart muscle came to be looked upon as the cause of anginal pain

In the course of investigations it was recognized that the P factor if not identical is close to lactic acid at least in many respects it behaves like lac tic acid (or phosphoric acid) For example lactic acid is known to cause pain in muscles when injected intravenously (Moore Moore and Singleton[?]) mus cular contractions will cease with the accumulation of the acid (Tennant [?]) and a high concentration of the acid depletes muscle glycogen Since lactic acid is neutralized by alkali ingested soda bicarbonate has been employed suc cessfully to retard the onset of pain in an arm when exercised (Katz[17]) These properties of lactic acid are almost interchangeable with those of the P factor

occlusion of coronary vessels observed in gradual obliteration of the lumen or in an organized thrombosis of long standing is not painful This statement however is not intended to ignore the vital function of collateral circulation, the relation of spasm to arteriosclerotic vessels is not clear

To some extent, but only to some, animal experiments lend support to the belief that a temporary mechanical constriction of a coronary vessel is painful We have in mind the signs of pain that attend the sudden rapid ligaturing (squeezing) of such a vessel Although Cohn[7] has argued that experimental traction on or squeezing of an animal s coronary vessel may not be identical with the spontaneous spasm of a human coronary vessel it would seem to us that it cannot be denied that all three events have a common denominator, namely, a physical mechanical element, and this regardless of any chemical chain of reactions The mechanics of spasm, therefore, may be common to artificial and spontaneous coronary constriction Wiggers [31, 3] objection or rather his reservation to the acceptance of the theory of spasm is more to the point He stresses that the coronary vessels contain very few muscle fibers for the development of sufficient tension to produce pain The induction of pain by ligating a coronary vessel or by tridirectional traction exerted on the vessel in one plane (Gorham and Martin[12]) probably depends on mechanisms other than tension of coronary muscle fibers A further criticism of the spastic theory is that in coronary spasm coronary flow may not be reduced after all, a position advanced by Wenckebach[30] on clinical grounds and indirectly suggested by the work of Lewis, Pickering and Rothschild[19] who found that blood vessels of ischemic skeletal muscle became dilated and developed an increased pressure Wiggers and Cotton[33] do not accept this

It will be noted that pain has here been described in terms of mechanisms outside the anoxic effect on the myocardium (p 6) a point of view emphasized again recently by Wyburn Mason [34] The theory of spasm of the coronary vessels cannot yet be abandoned

C *Myocardial Origin*

The occlusion of a coronary vessel is a mechanical event the significant results that follow from this are chemical This is true under natural conditions in man and in experimental practice on animals A coronary vessel that nourishes a section of heart muscle and removes metabolites from it cannot function when suddenly and tightly ligated The heart muscle is maimed and develops changes in electrical potential Electrocardiographic records of such changes resemble closely records obtained after an abrupt coronary closure in humans The logical inference is therefore, that in each case an ischemia of the cardiac muscle occurs This ischemia as we shall discover is conditioned by two opposing factors at least (a) a chemical alteration oxygen lack, or "P" factor (lactic acid production) in the muscle which in turn is minimized,

not thrombosed The systemic the constitutional features accompanying a reduction in coronary circulation a reduction which appears to be essentially functional in nature (p 1) as in the case of acute coronary insufficiency, and those which come with structural damage of the heart i e acute myocardial infarction are the expression in both instances we believe of autonomic activity varying only in intensity and duration It is not suggested that the reduction in coronary flow brought on functionally i e by vasoconstriction or by sudden blocking of the lumen of the vessels or the actual heart muscle damage precipitates the autonomic reaction or vice versa There is no settled knowledge on this point However it seems to be established that cardiac pain (and cardiac pain will be assumed to be a testimony of diminished coronary circulation) can be induced by stimulating a part of the autonomic system Leriche[9] brought on intense cardiac pain in human beings by stimulating the left stellate ganglion and Spiegel and Hashimoto[28] obtained the same result in dogs

III The Nervous Apparatus for the Initiation and Transmission of Pain

Our understanding of the initiation and transmission of pain has been altered and extended by the use of the cathode ray oscillograph This instrument based upon vacuum tube amplification will record the amplified action potential of nerve axons stimulated by pain The electrical potentials of sensory nerves are very minute and have different waves with respect to size shape and rate and differences also in refractory period in electrical excitability and in their predilection to travel in nerve fibers depending upon their diameter and the presence or absence of myelination On the basis of these criteria nerve fibers for carrying pain appear to fall into four general groups and of these two are especially concerned with pain in general and from our special point of view with cardiac pain

These two groups so-called C and B non medullated and small-sized medullated fibers are slow fibers that is they convey pain impulses at slow velocities about 15 to 60 per second contrasted with velocities of 100 to 150 per second from muscle spindles There is some evidence that fibers of the C group non medullated fibers are identified with dull lingering pain and fibers of the B group small medullated fibers with transient sharp pain In general however variations of intensity are due chiefly to an aggregate effect obtained by simultaneously exciting different kinds of fibers each with its own characteristic limit of velocity shape and size of potential waves[1, 8, 11]

No matter what kind of excitation thermal mechanical or chemical is applied to the nerve endings for pain these structures in reacting obey a constant law By this is meant that the electrical potential waves evoked are of a well defined range of frequency and of unchanged magnitude and form An increase in the intensity of the applied stimulus does not alter the size and shape of these waves nor their frequency beyond a definite rate For example a painful ex

The production of lactic acid or a "P" substance, however, is but part of the story, the other part depends, as already hinted, upon the circulation to the tissue affected The piling up or removal of metabolites is governed by conditions which either facilitate or prevent anoxemia (oxygen lack) A blood supply insufficient to prevent (by neutralization or physical displacement) the concentration of these chemicals above a certain threshold shares in the mechanism that incite the pain nerve endings to produce pain

A natural corollary is the alleviation or termination of pain in a muscle when its circulation is improved and the oxygen lack or debt in the tissue is thereby wiped out For anginal pain an adequate circulation or a blood supply ready to meet the urgent demands of impending ischemia of cardiac muscle is a sine qua non Pain, therefore, in the heart and its allied structures is determined and regulated by the accumulation and concentration of metabolic products and by the availability of adequate quantities of oxygen transported through the circulation (See Chapter I for anoxemia of heart muscle)

The painstaking studies of Blumgart and his co workers [5, 6] carried out on a large postmortem material of cases showing clinical manifestations of angina pectoris, coronary thrombosis and myocardial infarction, and congestive failure, led them to conclude that "the underlying mechanism in angina pectoris, coronary failure and acute myocardial infarction rests upon a relative disproportion between the requirement of the heart for blood and the supply of the coronary vessels' The extent and duration of the relative ischemia was responsible for the myocardial alteration, not the manner in which the change was caused This myocardial damage (infarction) and not the closure of the coronary vessels per se was responsible for the clinical syndrome designated as acute coronary occlusion and characterized by severe precordial pain, pallor and other features of shock and by well recognized electrocardiographic findings Extensive and minute examination of the autopsied hearts convinced the authors that in the human being an effective collateral coronary circulation is formed to meet the new demands consequent to myocardial infarction and that the sudden onset of angina pectoris or marked exacerbations in intensity or frequency of attacks of angina pectoris is presumptive evidence of coronary occlusion or progressive narrowing which has gone beyond the rate of development of coronary circulation Attacks of severe and enduring pain associated at times with collapse, were attributed to anoxia (ischemia) resulting from a prolonged insufficiency of blood supply to the heart muscle, in other words to a disproportion between the quantity of blood the heart needs and that which it receives This coronary failure' they go on to say may occur with or without simultaneous, or immediately preceding coronary thrombosis

If for the sake of argument one substitutes the condition acute coronary insufficiency for coronary failure' it will be appreciated that a wide range and intensity of symptoms may attend attacks in which the coronary vessels are

The second objection revolves about the concept that differences in the acuity and in the localization of referred pain are determined by the fact that sensations of pain are carried along many fibers converging upon common intraspinal central neurons whereas touch sensations are transmitted by fibers each of which makes a separate contact with an individual intraspinal central neuron It is difficult to accept this concept unreservedly because the common neurons in the spinal cord concerned with referred pain may well receive a converging group of sensory impulses from multiple foci on the surface of the body and yet fail to produce anginal pain

Impulses of pain have the smallest magnitude and their velocities are slow and intermittent yet pain from the heart and aorta often is rhythmic even constant A theory of the function of some amplifying device at work in the spinal cord and probably in the higher brain centers has been proposed to explain the registration into consciousness of pain as an intense and continued sensation The thalamus and cortex are recognized as receptors translators differentiators of pain whereas the lower centers especially the central synaptic junctions in the spinal cord according to Wiggers are supposed to fulfill the main amplifying function The concept of pain amplified in the neuraxis is not yet fully established

BIBLIOGRAPHY

[1] ADRIAN E D The Mechanism of Nervous Reaction Electrical Studies of the Neurone University of Pennsylvania Press 1932 Croonian Lecture The messages in sensory nerve fibres and their interpretation Proc Roy Soc London 1931-? *109* 1 The impulses produced by sensory nerve endings Part 4 Impulses from pain receptors J Physiol 1926-7 6? 33 Mechanism of the sense organs Physiol Rev 1930 *10* 336

[2] ALLBUTT T C Diseases of the Arteries Including Angina Pectoris London Macmillan 1915

[3] —— Angina pectoris New York M J 1922 *115* 181

—— Certain points in diagnosis and treatment of angina pectoris Lancet 1923 *I* 883

[4] BLUMGART H L SCHLESINGER M J AND DAVIS D Studies on the relation of the clinical manifestations of angina pectoris coronary thrombosis and myocardial infarction to the pathologic findings Am Heart J 1940 *19* 1

—— —— AND ZOLL, P Angina pectoris coronary failure and acute myocardial infarction The role of coronary occlusion and collateral circulation J A M A 1961 *116* 91

COHN A E Introduction to Diseases of the Coronary Arteries and Cardiac Pain ed by Levy R L New York Macmillan 1936

DALE H Transmission of nervous effect by acetylcholine Bull New York Acad Med 193 *13* 3 9

DOGIEL A S Die sensiblen Nervenendigungen im Herzen und in den Blutgefasse der Sau etier Arch f mikroskop Anat 1898 *5?* 44

—— Zur Frage uber den feineren Bau der Herzganglion der Menschen und der Saugetiere Arch f mikroskop Anat 1899 *53* 237

GASSER H S The control of excitation in the nervous system Harvey Lecture 193 109

[11] GORHAM L W AND MARTIN S J Coronary occlusion with and without pain Arch Int Med 1938 6 871

citation to these nerve endings produces a volley of impulses which is readily recorded as potential waves along the axons of the fibers connected to the nerve endings This volley or train of impulses travels at a slow rate, about *30 to 40 per second At this rate pain has an interrupted or pricking char*acter With a faster frequency, about 60 per second, pain grows continuous or smooth This change in rate takes place in axons that are the same (identical) and with no variation in magnitude or form of the waves, moreover, the velocity does not exceed its upper limit, 60 per second, and this increased rate is still slow compared with that of touch

The heightening or intensification of pain is accomplished, therefore, by variations in the rate of the frequency of the potential waves that pass along identical nerve axons except for this rate of frequency the waves undergo no change in range magnitude or shape The main cause of intensification of pain, it is alleged, is a spread of activity among an increased number of identical axons The intensity of pain, however, does not influence the duration of pain, pain does not linger merely because it is more intense Furthermore, the intensity of pain is not related to any increased acuity in its localization Heinbecker Bishop and O'Leary[14] demonstrated experimentally that an increase in the total number of nerve fibers carrying touch merely enlarges the area wherein the touch sensation is felt

Like referred pain from other organs, the coronary cardiac variety has two independent routes a visceral and a somatic, both active and with common focal points for the meeting of their impulses This hypothesis is well established in the literature As it stands, however, it has to overcome important objections only two of which we shall discuss at this point * First, as far as we know no one as yet has finally defined anatomically the central connections for pain in the entry zone of the dorsal grey matter of the spinal cord † Indeed, the zone of entry may be elsewhere [5] in the dorsal roots according to Pike (Chapters I and XI) The premise of mediation of reference in the dorsal grey matter ignores the fact that referred pain is nearly always radicular and that this type of distribution could hardly be inaugurated within the spinal cord where impulses would undergo diffusion through several segmental levels The referred pain that assumes on occasions, a diffuse character is *accounted for by Pike on the basis that mediation of reference* occurs in the dorsal root peripheral to its ganglion This again places the locus of convergence and mediation outside the cord with the actual mediation accomplished by a transfer of impulses or their effects from afferent visceral fibers to afferent somatic fibers, both types of fibers in the dorsal root lying juxtaposed and without a myelin sheath

* See Chapter XI for a fuller discussion

† Dogiel [9, 10] believes he found such connections but this does not exclude their existence outside the grey matter

CHAPTER XIV

Psychologic Aspects of Pain

I General Considerations

THE PSYCHOLOGIC concept of pain is complex and difficult to define in precise terms. Yet it is essential that we consider it not only as a biologic and physiologic entity and try to differentiate variously localized types of pain but also that we recognize its psychologic aspect from the standpoint of the physician and the viewpoint of the sufferer.

Pain cannot be simply defined because although it is found in the realm of sensation it is not clearly established whether it is a single specific sensation or whether what we describe as pain is a complex of several known sensations. In its simplest form pain would seem to be a reaction to unpleasant stimuli. Primitive animal forms respond by a reflex. Among the lower vertebrates the thalamus is a receptor organ for pain. In primates and in man the highly developed thalamic and cortical structures are the regions in which pain is not only received but registered and translated into consciousness.* Curiously enough the thalamus and cortex like the rest of the brain are themselves insensitive and serve only as the instrument through which pain is realized.

Pain varies in type and intensity; it has both qualitative and quantitative dimensions. A familiar example is the effect of friction on a portion of the skin. Gentle friction which may be neutral or pleasurable can readily become unpleasant or even exquisitely painful. The change is brought about by a quantitative increase in the stimulus rather than by any change in its nature. The cumulative effect of the stimuli causes a gradual transition from a pleasant sense of friction to one of pain. The same principle observed here in connection with a tactile stimulus can be seen in the case of thermal stimuli, i.e. warmth can readily become heat and this in its cumulative effect become painful. This re-emphasizes the idea already expressed—that pain is closely allied to thermal, tactile and compression sensations. But it is more than a physical reaction. There is always an accompanying emotional component, seemingly unpleasant.† This unpleasantness or unbearableness is so much part of the picture that oftentimes we gauge pain by our emotional reaction (emotional component) to it rather than by the merely physical aspects, i.e. the volume or strength or quality, etc., of the stimulus or the physical response of the organ.

* It is not within the scope of this discussion to attempt precise psychologic delineations of concepts such as consciousness, sensation, feeling. The terms are used in their accepted more popular sense.

† The pleasure sensation or gratification (libido) associated with pain are subjects which belong to psychiatry.

[13] HEBERDEN, W Some account of a disorder of the breast Med Tr Coll Phys London 1772 *2* 59
[14] HEINBECKER P BISHOP G H AND O LEARY, J L Pain and touch fibres in peripheral nerves Arch Neurol & Psychiat 1933 *29* 771
[15] HERING H I Die Karotissinusreflexe auf Herz und Gefasse Dresden u Leipzig 1927
[16] HEYMANS C, BOUCKAERT J J AND REGNIERS P Le sinus carotidien Paris G Doin 1933
[17] KATZ I N Mechanism of pain production in angina pectoris Am Heart J 1934 *10* 322
[18] KOCH E Die reflektorische Selbststeuerung des Kreislaufes Ergebn d Kreislaufforsch 1931 *1* 1
[19] LEWIS T PICKERING G W AND ROTHSCHILD P Observations on muscular pain in intermittent claudication Heart 1929-31 *15* 359
[20] LERICHE P La chirurgie de la douleur et ses résultats Presse Med 1927 *52* 497
[21] MONGE C L erythémie des altitudes Arch mal coeur *1929* *22* *641*
[22] —— High altitude disease Arch Int Med 1937 *59* 32
[23] MOORE R M MOORE R E AND SINGLETON A O JR Experiments in the chemical stimulation of pain endings associated with small blood vessels Am J Physiol 1934 *107* *594*
[24] PERLOW S MARKLE P AND KATZ L N Factors involved in the production of skeletal muscle pain Arch Int Med 1934 *53* 814
[25] PIKE F H An approach to the problem of pain fields with special reference to those associated with diseases of the nose and throat Laryngoscope 1928 *38* 219
[26] SPIEGEL E A AND HASHIMOTO S Über die Schmerzleitung aus dem kardioaortalen System in Beziehung zu den Spinalganglion und den Rückenmarksbahnen Ztschr f d ges exp Med 1930 *71* 408
[27] TENNANT R Factors involved in the arrest of contraction in an ischemic myocardial area Am J Physiol *1935* *113* 677
[28] —— AND WIGGERS C J Effect of coronary occlusion on myocardial contraction Am J Physiol 1935 *112* 351
[29] VAQUEZ H Diseases of the Heart Transl and ed by Laidlaw G F Philadelphia W B *Saunders* 1924
[30] WENCKEBACH K F Angina pectoris and the possibilities of its surgical relief Brit M J 1924 *1* 809
[31] WIGGERS C J The physiology of cardiac pain Chap 6 Diseases of the Coronary Arteries and Cardiac Pain ed by Levy R L New York Macmillan 1936
[32] —— Physiology in Health and Disease Philadelphia Lea & Febiger 1934
[33] —— AND COTTON F S Studies on the coronary circulation 1 The pressure pulses and their interpretation Am J Physiol 1933 *106* 9
[34] WYBURN MASON R A new conception of angina pectoris Brit M J 1948 *1* 972



gina pectoris the character of the pain is an outstanding feature It seems to be different from any other type of pain representing something distinct and apart from the physical descriptions of crushing vise like etc As a matter of fact aside from its horrible intensity, the pain is of such a nature that the sufferer finds no adequate words to characterize it

General considerations of the psychology of pain are but the background of the problem The more practical and individual details depend upon the other two aspects which belong in this chapter, namely the physician s ability to interpret objective and subjective evidence and the capacity and ability of the sufferer to feel and experience pain to react to pain to adjust himself to the onslaught of pain with all its curiously related emotional traumas and to the whole cycle of his life of which pain is a recurring feature

II The Individual Capacity To Feel and Experience Pain and To React to Pain

Psychologic as well as physiologic factors are vital determinants in the individual s capacity to feel and experience pain and to react to pain Compared with their role in the mechanism of pain (p 239) these factors here are less clearly defined and almost inseparable one from the other The capacity and the pattern of the reaction are however the result of more than these two factors Race heredity disposition qualities of discipline and training emotional endowment sex age and perhaps climatic and atmospheric conditions are also important

To disentangle these manifold influences is extremely difficult The task however appears to offer two avenues of approach an understanding of the known anatomic structures and physiologic mechanisms that pick up transmit and register pain and an appreciation of all the potentialities for function that are developed on this basis supplemented by important exogenous elements Unfortunately on all these points our knowledge is fragmentary but we can at least attempt a critical appraisal

As far as the problem permits therefore we must study pain (a) as a physiologic manifestation initiated and transmitted by the physical apparatus that exists in the body and (b) secondly as a psychologic reaction by the individual to the sensation or experience Sometimes the physiologic and psychologic elements appear to act simultaneously sometimes one precedes the other The physical apparatus consists of chemical transmitter substances acetylcholine and sympathin a rather intricate synaptic junction system in the cord and a receptor system in the thalamus and in the cortex The more recent studies in neurophysiology indicate that physical arrangements in this apparatus alone can account for quality and intensity of pain Quality of pain is achieved chiefly by an aggregate effect that follows a simultaneous stimulation of different types of pain fibers each with its own physiological effect (Wiggers[6]) Intensity of pain is determined by the rate of action waves set up

ism. A linkage of emotional and physical factors *is normal, in fact in severe* pain these two factors are scarcely separable and engender a feeling of revulsion. But that this revulsion (unbearableness) need not be an integral part of pain is proved by *the fact that in mild pain it is practically nonexistent.** Pain therefore, rests largely on a physical basis.

This physical basis is still further exemplified in the case of referred pain *from viscera, the heart for instance, by the feature of "amplification" of pain.* It has been suggested that referred pain is amplified in the synaptic junctional area of the spinal cord and perhaps in the thalamic and cortical regions. The *amplification may be physical and apart from any emotional reaction or the* element of shock, it is perhaps a frequent concomitant in anginal pain. Should the concept of an amplifying mechanism prove to be valid, it may contribute *to our understanding of how* it comes to pass that a comparatively small lesion—a thrombus, in what is after all a small vascular channel in the case of a coronary artery produces such terrific pain. On the other hand, the explanation may rest upon a *local* cause, i.e., a specialized threshold *for pain at the* cardiac nerve endings, or other factors.

The sources of pain, in general, are twofold: those which result from stimuli that impinge on the integument of the body and those which *have their origin* within the organs or deep tissues. The sensation of pleasure and pain from the integument or envelope of the body is a matter of great interest and concern to the psychiatrist, *especially* in its connotation *of generalized libido and* specialized areas of erotic reaction. The problem of intrabodily pain may take on almost a similar significance, i.e., the libidinization of internal organs. For the internist, *therefore, the general emotional aspects may become an important* field of interest. The individual with angina pectoris, for example, may be exemplifying a libidinization effect diverted to his heart when he is victimized by *emotional reactions which spring from anxiety, frustration, guilt or are* engendered by inherent or acquired psychologic forces set into action by the organic illness. These emotional reactions, according to Freud, are connected *with sexual instincts and drives retained in the unconscious, and often play* an important if not primary role in the total clinical picture. On the other hand the individual with angina pectoris may be concerned chiefly with a realistic *anxiety appropriate to the serious nature of the malady.* (See Chapter XX for psychologic aspects in psychosomatic disorders of the heart.)

The language is prolific in adjectives that are commonly used to describe *pain. This is evidence of its manifold aspects;* words such as boring, burning, piercing, twisting and countless others indicate the varieties of pain. These terms do not denote differences in degree of intensity, that is, they are not *quantitative* measures but rather expressions of qualitative variants. In an

* The role of the unconscious is not included in this connection.

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Psychologic as well as physiologic factors are vital determinants in the individual s capacity to feel and experience pain and to react to pain Compared with their role in the mechanism of pain (p 239) these factors here are less clearly defined and almost inseparable one from the other The capacity and the pattern of the reaction are however the result of more than these two factors *Race heredity* disposition qualities of discipline and training emotional endowment sex age and perhaps climatic and atmospheric conditions are also important

To disentangle these manifold influences is extremely difficult The task however appears to offer two avenues of approach an understanding of the known anatomic structures and physiologic mechanisms that *pick up transmit* and register pain and an appreciation of all the potentialities for function that are developed on this basis supplemented by important exogenous elements Unfortunately on all these points our knowledge is fragmentary but we can at least attempt a critical appraisal

As far as the problem permits therefore we must study pain (a) as a physiologic manifestation initiated and transmitted by the physical apparatus that exists in the body and (b) secondly as a psychologic reaction by the individual to the sensation or experience Sometimes the physiologic and psychologic elements appear to act simultaneously sometimes one precedes the other The physical apparatus consists of chemical transmitter substances acetylcholine and sympathin a rather intricate synaptic junction system in the cord and a receptor system in the thalamus and in the cortex The more recent studies in neurophysiology indicate that physical arrangements in this apparatus alone can account for quality and intensity of pain Quality of pain is achieved chiefly by an aggregate effect that follows a simultaneous stimulation of different types of pain fibers each with its own physiological effect (Wiggers[3]) Intensity of pain is determined by the rate of action waves set up

in the nerve endings in response to painful stimuli and transmitted along the same kind of fibers, C and B, to common synaptic connections Although this mechanism is important, the main factor in intensification of pain appears to be an increase in the total number of the same type of fibers, with no alteration in the velocity of their electrical waves

Leaving out of account for the moment what transpires in the process of the delivery of pain impulses from the central synaptic connections to the thalamus and to the cortex, it is clear that in the lower limb of the nerve arc, i e from tissues and organs to the spinal cord, there are anatomic and physiologic determinants of the quality and intensity of pain, and quality and intensity are practical criteria for estimating the individual response to pain

Diligent study is being directed to all three components of the lower limb of the nerve arc, nerve endings, axons, and synaptic connections, but we still lack information on the norm or standard of the quantitative relationship that exists between them The number of nerve endings may be subnormal, the arrangement of the axons not always the same for each person, or in a particular portion of the nervous system The chemical substances elaborated during impulse transmission are not fixed Moreover, we are ignorant of the exact *conditions by which groups of fibers other than C and B"* are called into action and our ignorance is no less with respect to the arrangement and functions of the common synaptic junctions It is therefore not possible to say whether quality and intensity of pain are not largely determined in *this portion* of the nervous system This ignorance renders it difficult too and perhaps even futile to appraise the influence of the higher pathways and centers For convenience, human beings in their response to pain have been roughly divided into three groups, normal (average) hyposensitive and hypersensitive These differences in response are undoubtedly attributable to the action of the higher as well as the lower centers but it may well be that the latter play a far more significant and important role than we have hitherto understood

The pathway from the central synaptic areas in the spinal cord to the thalamus and then to the cortex are also shrouded in darkness A few things however have come to light All sensations of pain reach the thalamus and *according to the neurologist many probably go no further* Lesions in the thalamus and in the cortex frequently are accompanied by emotional derangements These parts of the brain not only receive pain impulses translating them into consciousness, but function to achieve a kind of basal emotional *equilibrium* These structures are all important stations in the consideration of the individual response to pain To the physiologist thalamus and cortex are one instrument with the thalamus capable of affecting broad and general influences on emotionality, the cortex finer and preciser controls Both structures are looked upon as a physiologic unit in a manner similar to the consideration of the dif

fuse reticular zone spreading through the medulla pons mesencephalon and diencephalon by which control of physical and chemical bodily processes is accomplished Unfortunately very little is known of the interplay of forces between the thalamus and the cortex but there is hardly any doubt that emotional element as well as the intelligence residing supposedly in the cortex, have much to do with the response and reaction to pain in each case

The higher centers however and in fact the pathways that start at the junctional tissues in the cord the spino-thalamic tract possibly also sympathetic fibers in the spinal cord as well as extraspinal sympathetic and vagal routes all play a significant part in the reaction process of pain By the reaction process we mean the potentialities of function that are developed from this point i e junctional tissues on into very consciousness This portion of the cerebrospinal system has to do with every response that neutralizes diminishes or augments the effects of impulses of pain Moreover in these higher centers resides the capacity to differentiate pain, to experience its various tones as it were or to use another figure to distinguish various kinds of pain through consciousness as one recognizes the composition of light that passes through a prism

RACE

It is more than probable that different races* vary in their emotional responses and especially to pain There is some intimation that male Pueblo Indians and possibly Eskimos and Negroes also a number of primitive groups in various parts of the globe possess either a higher threshold for pain or are incapable of generating highly emotional states in the presence of pain or at any other time

In general the proof of inherent hyposensitiveness is difficult to obtain or appraise The inference that such a state exists in Negroes is based on the experience for instance that they often develop anatomic lesions that go with anginal pain and angina pectoris in other races and yet there are in this race proportionately few subjective accounts or objective observations of anginal pain (Paullin[1]) This infrequency is not entirely accounted for by the unreliability and inarticulateness of many Negroes in giving medical histories If the premise should prove valid that the Negro who is often very emotional is hyposensitive it would point to a nice and interesting distinction between sensitivity to pain and general emotionality Libman believed male Pueblo Indian were hyposensitive In this race however we must consider the factor of stolidity combined with discipline and tradition in other words Spartan qualities and perhaps above all the force of tribal opinion as a deterrent to the

* This term is here employed not in the anthropologic sense it designates merely well recognized human groups

display of signs of pain The power of this force Stefansson[4] has emphasized in a similar connection for Athapaska Indians and Eskimos Among these people, to show suffering is to lose prestige

In response to a request for information, Mr Desmond Holdridge[1] was kind enough to furnish the following comments

"I have been among Eskimos, Kjuka bush Negroes in Suriname, Neskopi Indians in Labrador, and various Indian tribes in tropical South America With Eskimos and Negroes I have noted nothing unusual in their manner of reacting to pain I have, however, noted again and again among Indians both in Labrador and in South America, a willingness to endure pain that on first sight is quite remarkable Almost all of the Amazonian tribes have hunting and puberty ordeals that involve a great deal of personal mistreatment that must be borne without evidences of pain, and as a general thing these tests are passed successfully But that this apparent insensitivity is due to a nervous peculiarity I can hardly believe Rather I would trace it to environment and upbringing which brings about an attitude of stoicism

As an example of the influence of this attitude, I had often noticed that an Indian hunting might stand on a nest of ants or astride a large column of ants while close to game, and make absolutely no sign of the intense pain At first I was quite admiring, but later I found that when sufficiently interested in hunting myself and accustomed to the Indian example, I was able to do precisely the same thing letting ants bite me without disturbance and even getting a perverse kind of pleasure from it, and I am no stoic "

Hyposensitiveness should not be considered a deficiency, it is rather an endowment and is not to be confounded with stoicism, a state wherein a practiced self control simulates lack of capacity for emotional response A mild subjective response in these races therefore, calls for special caution in anginal cases The mildness of pain is no gauge of the serious import of the malady and this is equally true of the absence of pain

Hypersensitiveness is comparatively common in some racial groups It is of course dangerous and misleading to label an entire people as hypersensitive, or for that matter to endow them with any special characteristic, although it would seem that the Latin temperament and the Semitic groups, Jewish Arab etc , for example, are more likely to have their emotions touched off by pain It is not established that environmental rather than inherent elements evoke the reaction

Heredity and Disposition

Emotional response to pain is however, governed also by the inherited make up of each individual A patient born of strong sturdy emotionally stable forebears has an advantage in coping with angina pectoris The emo

tional equilibrium he inherits often will save him self inflicted fear and anguish that the over apprehensive individual suffers For want of a better term we speak of the inherited disposition of a human being as placid phlegmatic amiable happy or explosive aggressive irascible sullen These kind of dis position are bound up with psychologic traits and especially with introversion or extraversion of mind and spirit

There are of course inherited physical factors upon which the emotions depend for example hormonal secretions in the body that undoubtedly share the cause of the manner in which an individual is provoked by pain and reacts to it Inherited and acquired physical somatic and emotional or psychic forces are interlocked and fashion the various kinds of response to pain

Environment and Training

The response to pain is subjective as well as objective we have already com mented rather extensively on the objective reactions (Chapter II) The be havior of the anginal sufferer in the presence of these objective signs will often depend on his capacity to control his subjective reaction The objective signs conform to fairly well recognized clinical pictures and are in keeping with the physical nature of the malady Objective and subjective features combined form the total expression of the way in which any anginal sufferer acts

No elaboration is necessary of the power of the subjective features or emo tions where pain is concerned It is not the same for every individual and broadly viewed differences rest not only on racial and hereditary attributes to which those of sex and age may be added but upon factors of environment and training

Stoicism and tolerance are elements often evoked in the reaction to pain They are not necessarily inherent qualities though it must be admitted that one cannot draw too fine a line in this respect Stoicism is a form of disciplined self control and represents a kind of protective armor fashioned by the psyche to ward off the penetration of pain This is distinct from tolerance or bearable ness which may be defined as the equivalent of reserve upon which the individ ual draws to withstand pain that might otherwise be annihilating or beyond his control This idea of reserve is comparable to the alkali reserve in the blood or to cardiac reserve which act as reservoirs in time of urgent need The capacity to bear pain what the psychologist term bearableness is not to be mistaken for an attribute of the physical mechanism involved in react ing to pain

The acquired factors of environment and training are quite apart from in herent physical differences in the nervous apparatus by which individuals may or may not be able to withstand pain or permit its entry into consciousness Guidance in infancy childhood and adolescence the preparation for the chal

lenge that meets the individual during these stages and later adult life develop, or at least ought to develop, qualities of discipline and fortitude An environmental existence reasonably adapted to the individual's potentialities should produce an emotional equipment adequate to face affliction and pain with sound sense, free of ascetic martyrdom or of indulgence and self gratification, even with calm and equanimity in many cases A philosophy that recognizes the futility and the deep martistry of fighting inexorable biological laws and that accepts the inevitability of certain problems will save the individual from wasting his emotional strength This does not imply an attitude of fatalistic defeatism

All this is not accomplished by exhortation on the part of the physician or by girding up the loins on the part of the patient A long antecedent period *of child and adult training is a prerequisite or, in fortunate instances*, a natural gift of wisdom The practical bearing for the anginal sufferer is that all this supports him if the pain is not too overwhelming and devastating to prevent him from replenishing his strength from the wells of his emotional reserves It enables him to contrive and develop distractions with which to throw off or soften pain It colors his outlook on life, safeguarding him from unwise exertion and sharpening, within his own restricted limits, his individual capacity for adjusted living during the intervals free of pain An adjusted human being should not fear death nor live in apprehensive wait of death or pain and during the waiting process miss his opportunity to live in the fullest and best sense as far as he is able The invalidism of anginal patients is by no means a time of total loss for living As is well known, the anginal victim who so often comes so close to death learns to appreciate life and savor its best with moderation and a keener sense of awareness The degree to which this can be attained is however unfortunately governed all too often by the acquisition of peace of mind that comes from social and economic security All this is true not only for anginal sufferers but for many patients afflicted by other serious forms of organic heart disease

Another aspect of the armamentarium which environment and training forge is reflected in an attitude of resignation This strange reaction is at times the outgrowth of deep religious feeling and not necessarily an escape from reality At its best it is an indication and expression of emotional equilibrium achieved without terror and without frustration and guilt This attitude is an invaluable bulwark against the mental ravages of anginal pain or severe distress associated with fear and anxiety It is hardly to be expected in younger people who are more likely to be embittered and resentful of their premature incapacitation but in older persons too a quieter resignation is by no means the rule In fact those with cerebral arteriosclerosis frequently develop irascibility and an abnormal tendency to struggle against the inevitable

Atmospheric and Climatic Conditions

These are difficult to evaluate It is common experience to hear of a lighting up or aggravation of various kinds of pain during inclement weather or in climates that tax the resources of some individuals Unfortunately no exact studies exist on this point As nearly as one can tell the influence on pain is not due to electric conditions of the atmosphere as in bad' weather storms etc but rather to excessive variations in humidity

Classification of Individuals With Respect to Pain

Pain is a valuable yardstick with which to measure the emotional and mental equipment of most patients The capacity to differentiate pain resides in the higher brain centers notably the cortex and perhaps the adjoining subcortical territory Human consciousness is capable not only of recognizing pain but can differentiate nuances and modalities of pain By virtue of consciousness the will to do and the will to live pain may be narrowed or deflected or disregarded Distraction discipline training bear on this problem as we have already observed but the mind is also able to develop substitutive reactions that repel retain or qualify pain All these factors relate to and condition or fix the individual s capacity for experiencing pain

The reaction to pain and practically speaking this alone is at present our reliance for placing all human beings into the three groups already mentioned hypersensitive or overactive hyposensitive or underactive and a middle or average group This classification is but a rough expedient and leaves much to be desired

a The hypersensitive group The first the hypersensitive group comprises individuals who are apprehensive overanxious and whose reaction to pain is usually exaggerated The pain is not imagined there is no question therefore of its validity but in such individuals an uncontrolled imagination may arouse unwarranted emotional emphasis The emotional component *is not* only marked but may dominate the scene physiologic manifestations taking a secondary or even neglected place It is surmised though by no means proved that the higher brain centers of such patients are hypersensitive that is to say trigger ready and overactive when they are touched off The physiologic activities which do not go higher than the spinal centers do not evoke an emotional component since the higher parts of the brain concerned with consciousness are not involved The lower neuron system however has its own threshold for picking up and transmitting pain but it is not known whether this lower system too may become hypersensitive in the same way as the upper centers

b The hyposensitive group In hyposensitive people the reverse seems to be true The upper centers are low and sluggish to act and their response is slight or negligible The emotional accompaniment is therefore feeble or

submerged Since the upper centers are not called upon, the lower pathways and centers are probably chiefly responsible for the subnormal reaction in general, and for the special patterns of radiation, etc that are encountered in these subjects This is by no means fully established and indeed the entire relationship of psychologic to physiologic factors requires much more study

The usual forms of pain in this group their reference the substitutes and equivalents for pain have been studied by Libman He recognizes types in general by applying a simple test which he devised In his own words "in performing the test, it is important, after one has exercised the control pressure upon the mastoid process and proceeds to press in the direction of the styloid process not to also press upon the ramus of the lower jaw There exists a naturally sensitive point at about the middle of its border, and when this is pressed upon, in addition to the sensitive point behind it, the patient, if at all sensitive to pain, responds more than if the usual point alone is examined" The pressure is exerted upon a branch of the auricularis magnus nerve

According to this author the hyposensitive subject whom he recognizes by this method will not only feel little or no pain when afflicted with conditions that usually produce cardiac or anginal pain but whatever cardiac pain he has, is much more apt to exhibit greater radiation he is more likely to have reflex symptoms as well as substitutes or equivalents for pain Mild pain or absence of pain occurs in other groups, but in the hyposensitive patient it is practically the rule, at least intense pain is not a frequent incident The radiation is on the left side this may be looked upon as the same side in which the lesion exists, or the radiation may be contralateral "Inverse" radiation, or perhaps better expressed, a reversal of the direction of radiation, is considered characteristic of the hyposensitive state e g, referred anginal pain may begin in the little finger or wrist and spread to the pectoral and sternal areas Furthermore, the hyposensitive state is supposed to be more prone to develop reflex symptoms in angina pectoris in the presence or absence of pain

It is claimed that this group exhibits a greater propensity for developing substitutes and equivalents for pain dyspnea, not a usual feature in angina pectoris (apnea instead) is outstanding with pain secondary or completely supplanted or covered up by the dyspnea Vertigo may take the place of pain or of nausea and vomiting and instead of pain the victim will complain of heart weakness or profound general weakness or heavy fatigue As a rule the severe local pain of the sensitive individual is absent Other substitutive symptoms of anginal pain of a noncoronary variety are a feeling of pressure a weight in the chest, thermal sensations burning or severe cold in the chest or in radiated areas a sense of constriction in the throat or chest, or a feeling of fullness in the arms forearms etc

c Between the hypersensitive and hyposensitive groups are those who when afflicted with anginal pain exhibit reactions which go to neither extreme

This does not mean that patients in this group will not suffer from gradations of pain, but whether mild or intense the whole picture of their reaction is in harmony with the degree and duration of the pain experienced They differ more especially from hypo ensitive individuals in that they respond in the average normal way to Libman s pressure test It is possible though for a paroxysm of angina pectoris to seize them and cause little or no pain

BIBLIOGRAPHY

[1] HOLDRIDGE, D Personal communication.

[2] LIBMAN E Tr A Amer Phys. 1926 41 305 1929 44 57 Observations on individual sensitiveness to pain J A M A 1934 102 335 Symposium Angina pectoris with special reference to coronary artery disease Bull New York Acad Med 1935 11 427

[3] PAULLIN J E. Tr A Am Phys 1927 42 46 Confirmed by Thayer and Longcope (In the discussion of this paper Paullin and Thayer stressed the difficulty of eliciting a history of anginal pain in the Negro)

STEFANSSON V Personal communication

[5] WIGGERS C J The physiology of cardiac pain Chap 6 Diseases of the Coronary Arteries and Cardiac Pain ed by Levy R L New York Macmillan 1936 Physiology in Health and Disease Philadelphia Lea & Febiger 1934

The following additional references bear on the text of this chapter

BURNETT N C AND DALLENBACH K M The experience of heat Am J Psychol 1927 38 418

HARTSHORNE C The philosophy and psychology of sensation Chicago University of Chicago Press 1934

KNIGHT L The integration of warmth and pain Am J Psychol 1922 33 587

NAFE J P Summary in Murchison s Foundation of Experimental Psychology Worcester Mass and London Clark University Press 1929

STRONG C A The Origin of Consciousness London Macmillan 1918

SECTION SIX

Psychosomatic Disorders of the Heart

CHAPTER XI

Psychosomatic Disorders of the Heart

Introduction

To COMPREHEND psychosomatic disorders which involve the heart it is necessary to have an understanding of psychosomatic disorders in general Accordingly in this chapter some of the general principles of these conditions will be discussed and inasmuch as this volume is chiefly concerned with the behavior of the autonomic nervous system in relation to angina pectoris and myocardial infarction the discussion will center on psychosomatic disorders which may simulate these conditions The remarks which follow are however equally relevant to other forms of heart disease

Although the term psychosomatic signifies an ever present interdependence between psychological and somatic factors and thus implies that every condition in health or disease is psychosomatic, it is nevertheless true that the attempts to single out certain conditions and diseases under this designation have the advantage of always directing attention to both factors when *one or the* other might be ignored These factors not only affect each other but together achieve a dynamic equilibrium of the activities of the mind and body and to a great degree these activities are controlled by the autonomic nervous system

We shall in this chapter touch upon certain aspects of the autonomic nervous system even though they have received rather full attention earlier in this volume These aspects comprise the flexibility of the autonomic dynamic equilibrium the mass action of the autonomic apparatus as a whole and its related patterns of clinical disorders and disease and the process of referred pain Before however considering these features we shall briefly review several relevant psychological processes

Psychological Aspects

A most important element in the psychogenesis of psychosomatic disorders is the emotional tension which builds up in the individual The small conflicts and tensions inherent in daily living are usually quickly resolved but they may become intensified and augmented and find no ready outlet Emotional disturbances may be acute dramatic and violent as in rage or fear or insidious and subterranean in the form of guilt anxiety and therefore less obvious

Emotional Reactions and Autonomic Activities

The strong emotional upheaval of excitement or rage, accompanied by a multitude of physiologic reactions can be relieved just as quickly and dramatically as it came by utilizing the voluntary or skeletal musculature and the sensory perceptive system Motor acts brought into play in a fight will greatly decrease and even obliterate emotional tension The heat of battle over and anger cooled, the autonomic activities which accompany the emotional storm rapidly return to normal and no emotional residue is left behind to stimulate the autonomic nervous apparatus

Frequently, however, the individual is the victim of slowly piled up conflicts which lead to emotional pressure This pressure is kept up by recurrent psychic stimuli which induce a state of general autonomic excitation Since the physiological accompaniments of autonomic hyperactivity are themselves incapable of relieving tension the subject becomes a victim of emotional and bodily disturbances, these are termed vegetative neuroses Essential hypertension and chronic hyperchlorhydria are held to be examples of autonomic or vegetative neuroses

Emotional Reactions and Conversion Hysteria

In many cases, however, an inner or unconscious* urge for relief of the retained emotional tension will not down and the patient often resorts to a conversion mechanism to obtain relief The mechanism consists of unconsciously *projecting complaints and symptoms into various regions or organs* of the body For this purpose he employs the same apparatus i e, the skeletal musculature and sensory perceptive system but since its use is partial and ineffectual the result in terms of relieving tension, is inadequate In short although *he seeks outer means for expressing the need to reduce his inner tension* these means are weak substitutes for the vigorous and full acts of the somatic systems For example the deep unconscious impulse to secure relief or to protest or cry out may take the form of a dysfunction of the larynx or bronchial musculature or an inability to walk as in hysterical paralysis of limb muscles

Ineffectual as these symptoms are they nevertheless represent a kind of instinctual urgency and are symbolic of this need The symbolism attaches to the process, i e modus operandi by which the symptoms penetrate to a particular organ and not to the signs and complaints in terms of the organ involved

Attempts have been made to distinguish conversion hysteria from autonomic (vegetative) neuroses on the basis that the former is usually free of autonomic activities, but psychiatrists are well aware that such a distinction is not always possible To begin with the patient with conversion hysteria may actually suffer from emotional stress which inaugurates autonomic reactions as

* This word is employed in its psychodynamic meaning

in other subjects Moreover, the psychoneurotic may undergo autonomic activities expressed as physiologic reactions in various organs including the one that is the recipient of the conversion symptom This kind of symptom therefore may or may not be associated with general autonomic hyperactivity In any event the conversion symptom although at best an incomplete and futile attempt at relief represents an unconscious requirement and a source of satisfaction Abetted by the conviction that a tissue or organ is diseased the patient gives dramatic import to his signs and symptoms and thus procures some measure of gratification

Emotional Behavior and Infantile Mechanism

Psychosomatic disorders possess a strong etiological basis of regressive or infantile attitudes and emotional traumas These disorders are in a psychodynamic ense disorders of infancy namely they conform chiefly to the instinctual and emotional life that starts in the pregenital period and continues into adulthood The concentration of the patient s interest or energies on somatic features is accompanied by a strong unconscious wish to withhold from view infantile emotional motivation and behavior This appears to be the case in persons who have a disordered physiology i e functional disturbance involving the autonomic nervous system who have organic disease or who through a personality defect cannot cope with physical illness

AUTONOMIC MASS ACTION* IN PSYCHOSOMATIC DISORDERS

Physiologic Responses

The entire autonomic nervous apparatus functions as a unit i e as if all its central representations were set in motion These representations extend throughout the spinal cord medulla pons mesencephalon diencephalon and for the most part consist of aggregations of cells nuclei with rather well defined anatomic boundaries and specific physiological functions Some nuclei or centers are less clearly defined anatomically and distinguished almost wholly by their physiologic properties All the areas or centers together may be touched off as a unit by a variety of stimuli and the effects of the reaction are transmitted by a vast number of efferent sympathetic and parasympathetic pathways to all parts of the body

Once an emergency state is met by fight or flight the autonomic responses return to normal and the emotional tension practically disappears Autonomic responses set off as part of an autonomic mass reaction are however brought into play by emotions other than fright or anger These responses are likely to be less marked and widespread and as already mentioned are usually without effect as far as ridding the body of emotional tension goes

* A fuller exposition of this subject will be found in Chapter IV

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* This word is employed in its psychodynamic meaning

in tance The initial emotional provocation may range from lethargy to excitement and rage or from grief frustration to joy and other emotional experience

The Tonic State of the Emotions

A normal human being is probably never devoid of emotions Just as the dynamic or tonic state of the body is determined by physiologic and psychologic factors so too psychogenic and physiologic elements determine the dynamic or tonic equilibrium of the emotions The body possesses mechanisms in the physiologic realm which function at levels that are trigger ready to react they do not start at zero or at zenith and a similar provision holds for the emotions (p 76) Chemicals hormones and other agents participate in the preservation of the emotional dynamic balance but the chief control devolves on the cortex and adjacent subcortical territory In conjunction with other areas of the neuraxis they function as a whole to establish an emotional equilibrium i e a tonic emotional state

The fu tion of the cortex The cerebral cortex (neopallium) has autonomic representations of its own but it exercises a supervisory inhibitory power over the broader and less discriminative functions of the lower archaic brain centers It posses es also an excitatory effect on many activities of the brain stem Despite this dual action the cortex in the aggregate holds the activity of the lower older centers in leash and gives their activities a finer sharper focus

There is little doubt of the interaction between cortical processes (will power intellect discipline conditioning) and the deep pseudoaffective reactions which are demonstrable in animals deprived of cortex and thalamencephalon (p 736) An interaction also exists between cortical processes and emotional states such as anger experienced in full consciousness The cortex is the repository of highly organized processes with which in the form of consciousness will power d scrimination the individual can shield himself or modify and fend off emotional onslaught The supervisory or restraining influence of the cortex exe cised on emotional states engendered in the cortex itself or in deeper cerebral regions the hypothalamus particularly is very great Were this not the case violent and explosive reactions without semblance of control would be touched off by trivial provocation and the tumult and intensity of these attacks could be devastating In man for example the cortex acting as a damper and rheostat for the hypothalamic region permits the slow and orderly evolution of shades of mood and feeling The gradient so to speak of emotion is steady and progressive not necessarily disruptive and bounding The normal full grown individual develops adaptive reflexes with which to meet the strain of an emotional storm To lose one s head in an emergency means literally the loss of cortical faculties This point of view is also supported by experimental evidence in lower forms For example in the cat and dog reactions of unwar

The autonomic mass action induced by psychic stimuli differs in no respect from that produced by other types of stimuli The general and peripheral reactions are coordinated and give rise to a clinical picture which may be mild or intense, brief or prolonged intermittent, regional or wide flung Under some conditions as in excitement, the adrenergic or sympathetic adrenal activity is to the fore, under other circumstances, as in lethargy approaching sleep, the cholinergic or parasympathetic influence is ascendant and dominant

A large variety of emotional stimuli may disturb the autonomic regulations and these are registered as central and peripheral effects producing deviation in heat or water exchange, metabolism, circulation, respiration, gastrointestinal and genitourinary functions, sweating and pilomotor acts, sleep-waking rhythm These disturbed activities make up in a variety of combinations, the clinical patterns of disease Since an autonomic mass action is common to them all, it is not surprising that varied and unrelated conditions, as for example cerebral apoplexy acute coronary occlusion, and even food poisoning, may resemble each other and even defy clinical differentiation This principle is valuable in appraising the nature of cardiac manifestations produced by organic lesions in other parts of the body

Emotional Factors

A great many psychosomatic disorders are examples of an exaggerated or subnormal autonomic activity which has not gone on to produce morphologic damage Prolonged, marked, frequently recurrent autonomic disturbances as already intimated, need not cause tissue damage Witness the chronic recurrent condition of neurocirculatory asthenia or observe the palpitation essential hypertension or spastic phenomena that recur and endure over years and yet lead to no structural injury A chronic or oft repeated state of emotional tension may however set up morphologic alteration A classic example is peptic ulcer The ulcer or crater is the somatic consequence of a stomach under a protracted neurogenic bombardment instigated by emotional factors The ulcer does not relieve the emotional tension on the contrary it may add to it Nor has the ulcer any connotation of a wish for self punishment or self immolation since it is devoid of any psychodynamic implication of symbolic expression The morphologic destruction i e the peptic ulcer may however serve as a useful gauge of the fluctuation of the unrelieved emotional tension or conflict

The autonomic disturbances of the body induced by emotional factors are in turn capable of arousing superadded emotional phenomena For example fear may be the original precipitating cause of a general autonomic reaction but the associated change in the behavior let us say, of the heart bowel larynx can cause further fear and anxiety Fear therefore will engender new fear derived from the symptoms and complaints in the organ involved the heart for

Each organ possesses a supply of afferent *sympathetic* fibers which goes to a specific number of dorsal roots and then to the substantia gelatinosa in the cord In most individuals these fibers converge predominantly upon a limited number of dorsal roots and then travel to corresponding cord levels For example the preponderance of convergence and entry of afferent sympathetic fibers from the heart is at the levels of Th I to 4 on the left side from the gall bladder at the cord levels on the right side of Th 8 and 9 perhaps 7 This rather sharply defined concentration of afferent autonomic visceral fibers accounts for the particularity with which as a rule each organ announces visceral pain into its related dermatomes

The second set of the dual system of pathways consists of afferent *somatic* fibers which connect each group of dermatomes related to a specific organ to the substantia gelatinosa in the cord The concentration of somatic and visceral autonomic fibers upon common cord levels makes possible the reference of pain from an organ into its related dermatomes For the mediation of cardiac referred pain the afferent somatic fibers travel in the left *intercostal nerves of Th 1 to 4* for pain referred from the gall bladder the somatic fibers run in the right intercostal nerves of *Th 7 8 and 9*

While referred pain in the greatest number of instances depends upon the entry of the bulk of afferent autonomic fibers from the organ in question into a *limited* number of cord levels it seems to be also true that multiple accessory groups of afferent (autonomic) fibers from the organ may reach still other cord levels Such fibers are outside the zone of concentration and are usually too few *or too diffuse* to transmit any appreciable quantity of sensory impulses of pain but the fibers can under certain circumstances transmit much or most of the impulses into the neuraxis The existence of these groups enlarges the potentiality of any viscus for bringing into action many cord *segments which are* otherwise uninvolved

Psychosomatic Cardiac Disorders

General Considerations

It may be asked why is the heart so frequently a target or offender in psychosomatic disorders? Probably as in the case of the child s gastrointestinal tract subjected to food mixed with the parents emotions the cardiovascular system too is readily *affected* in early life by emotions and the neurogenic devices by which the cardiovascular apparatus is regulated are always *responsive* to emotions

It has been claimed that *certain* individuals with a special personality profile which includes many *constitutional* features are more prone to develop psychosomatic cardiac *symptoms* This touches on the entire problem of

ranted ferocity are produced when the restraint of the cortex or the influence of the forebrain are disturbed or removed.

The function of the hypothalamus. This region and the adjacent subthalamic territory are closely related to the regulation of the sleep waking rhythm and to certain aspects of lethargy. Lethargy and somnolence follow damage of this part of the brain. The emotional components of lethargy and excitement are in reality not neutralized but combined and integrated so that either element gains ascendancy under suitable conditions.* In animals, angry behavior as well as sexual excitement have been elicited by stimulation of the hypothalamus.

Referred Pain in Psychosomatic Disorders

When a patient is undergoing a generalized (total) or even a lesser degree of autonomic mass reaction, the distribution and pattern of referred pain will often indicate the specific organ responsible for the reaction (p. 226). On the other hand, although in many instances a psychoneurotic may appear to have, in addition to generalized autonomic responses, referred pain with respect to his heart or any other organ, a careful investigation may disclose that the character of the pain and the absence of contiguity of dermatomic involvement point away from referred pain. A somatic disturbance or lesion is not to be held responsible for what appears to be but actually is not referred pain.

It is profitable to recall in this connection that many thoracic and even lumbar cord levels may participate in the mediation of pain from any single viscus. This accounts for the propagation, for instance, of cardiac pain into unrelated, i.e., noncardiac dermatomes and, what is even more important to the student of psychosomatic medicine, explains the behavior and registration of noncardiac pain into cardiac dermatomes (Chapter XI).

These physiologic and autonomic considerations only serve to emphasize the practical need of determining whether simulated anginal referred pain, to take but one example, originates in a noncardiac lesion or is evoked solely by a psychic process. The clinical cases cited below (p. 256) bear on this subject. For convenience, a brief description of the mechanism of referred pain is included at this time, even though a fuller account has already been given (Chapter XIII).

Referred pain depends essentially upon the participation of a dual system of afferent pathways, the one somatic, the other autonomic. Impulses carried by each system converge upon common cord levels.

* The reader is cautioned against concluding that the problem of emotional response in relation to brain structure is clear or simple. Enough, however, is known to indicate that emotional excitability and angry behavior, as well as placidity and stolidity, have their anatomic cerebral representation. Moreover, the experimental results are not the same in all mammals; damage of the forebrain structures gives rise to angry behavior in the cat, but the opposite effect in the monkey.

possesses fairly well-distinguished features Its origin distribution and mechanism have been considered at length in Chapters XI and XIII Cardiac pain in psychoneurotic subjects however is frequently nonanginal in character

Psychosomatic cardiac manifestations may be divided into those observed (1) in subjects with a normal heart and (2) in subjects with a diseased or disturbed heart.

*Manifestations in Subjects with No Organic Heart Disease**

The neurotic individual free of organic heart disease but enraged or greatly excited exhibits general autonomic manifestations and cardiac features such as rapid or irregular heart rate and often cardiac pain which is referred If the individual is neurotic a victim of anxiety frustration, or guilt the cardiac manifestations may make up almost his total concern with general autonomic features such as sweating salivation glycosuria insomnia minimal or absent or the general autonomic features may be fairly well marked Neither cardiac nor general manifestations bring emotional relief as a rule and they subside when the emotional pressure is reduced A paradoxical condition is noted in some patients the cardiac complaints are diminished in the presence of increased emotional tension and aggravated when the patient is comparatively free of emotional strain

The angor animi or Todesgefuhl i e the terrorizing realization of impending death characteristic of angina pectoris or acute myocardial infarction is absent Furthermore the cardiac symptoms provide the psychoneurotic with justification and a certain comfort of mind He feels he has gained a solid foundation for his complaints and apprehension and what could better serve this purpose than an affliction real or imagined of an organ as vulnerable as the heart This sense of affirmation often makes it extremely difficult to separate the subject from his complaints and symptoms among which pain in the heart or in the region of the heart may be most prominent

Nonanginal Cardiac Pain

Pain in the heart or heart region is frequently encountered in subjects who have no organic heart disease *This* type of pain seems to fall into four main groups (1) pain *in* the heart or heart region produced by lesions in organs other than the heart (2) pain in the heart or heart region caused by physiologic reactions as in a generalized autonomic mass reaction precipitated by severe fright or anger (3) pain in the heart or heart region manifested as a conversion symptom and (4) as a deliberately malingered complaint

1 *Pain in the heart or heart region produced by extracardiac lesions* This form of pain may be referred to the heart region is often transmitted into cardiac dermatomes and is usually accompanied by general autonomic manifestation

* Organic heart disease was excluded on the basis of the patient's history physical examination electrocardiogram and fluoroscopic examination

specificity in psychosomatic research.* One group of students maintains that *emotional tension induced by any cause* may affect any part of the autonomic system, that if the subject is already conditioned by a weak or disturbed organ it will behave as a shock organ and react to any and all emotional provocation. Another group contends that autonomic dysfunctions will follow specific emotional stimuli and supports this premise with the argument that the physiological responses to different emotional tensions are varied. Recent investigators have urged that the psychologic background of emotional diarrhea or constipation is not the same as *in gastric neurosis and that cardiacs are* unlike asthmatics in this respect.

That the heart and emotions are closely connected is a tradition older probably than recorded history. The heart as well as the bowels have long been considered repositories of compassion and kindness, wrath and rage. Indeed *many viscera have been associated with emotional qualities the spleen with* anger, the gallbladder and the biliary system with hostility, the kidney with aggression. The heart however and the entire cardiovascular system eventually came to be regarded as an actual as well as literary and poetic vehicle and instigator of emotional reactions, and it was noted that the heart could function in this respect whether it was sound or maimed.

Generally looked upon as a vulnerable, delicate organ whose failure may mean suffering or dissolution, it is quick to feel its owner's mood, apprehension or anxiety, and like all other organs of the body it is the recipient of autonomic activities induced by the psyche or body. Like other organs too it appears to serve as an object for a conversion symptom. The symptoms in either case may be focused almost wholly in the cardiac apparatus. Finally the heart may, by the symptoms aroused in it aggravate and magnify pre-existing anxiety and thus complete a vicious circle.

Cardiac Pain and its Simulation

One of the strongest links in the chain of events which keeps the psychoneurotic attached to his psychosomatic disorder is cardiac pain. Many psychoneurotic subjects are alert to the forms and guises that cardiac pain assumes and are likely to employ this knowledge unconsciously to confound and alarm physicians and relatives. This form of motivation is not duplicity or *calculation* as in the malingerer. The patient furthermore, soon comes to look upon his symptoms, pain in particular with a sense of personal possession and he will fight for the validity and retention of his complaints and symptoms even in the face of authority. In all psychogenic disturbances associated with pain in the heart or the heart region anginal pain must be excluded. *This form of pain is* produced by disease or physiologic disturbance in the cardiac apparatus and

* The question of *specificity in general and its bearing on the heart* is beyond the scope of this volume. Psychoanalytic studies indicate that specificity is bound up with deep dynamic psychologic factors.

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of the same kind and degree observed in angina pectoris or acute myocardial infarction Acute gallbladder disease, acute esophageal herniation, acute pulmonary infarction (post phlebitic) are examples of such noncardiac lesions The combination of a severe autonomic upheaval and pain referred into typical cardiac dermatomes will naturally arouse the suspicion that the acute episode is of organic cardiac nature But if such a suspicion is not tenable as, for example, in young subjects with a sound cardiovascular apparatus, the physician may be led to believe that the attack is hysterical The latter diagnosis however should be considered only when organic disease has been carefully excluded Examples of the simulation of anginal pain due to organic extracardiac conditions will be found in Chapter XII This type of pain can also occur in neurotic subjects, in whom it must therefore not be mistaken for a neurotic complaint

2 *Pain in the heart or heart region caused by autonomic activities* Although it can not be said with certainty that autonomic activity will produce cardiac pain in subjects who have normal coronary vessels and myocardium there is suggestive evidence that tends to support such a possibility For example, it is recognized that the autonomic mass reaction noted with fright or anger will liberate undue amounts of adrenalin and that this substance can raise arterial blood pressure to high levels and thus throw a severe strain on the heart Theoretically at least such a strain, accompanied perhaps by a tachycardia which results from stimulation of the cardio accelerators might be sufficient to upset the autonomic regulation of the normal coronary circulation in a young subject who possesses a sound cardiovascular system Pounding throbbing sensations in the heart, and even cardiac pain are not unknown in such subjects after the parenteral injection of fairly large amounts of adrenalin or after intense emotional stress It is however, not yet determined whether milder forms of autonomic activity are able to produce similar sensations in the normal heart

3 *Pain in the heart or heart region as a conversion symptom* The character of the pain and its mode of onset and reference into the integument are not related to exertion or emotional strain The pain is transmitted into dermatomes that are irregular and bizarre and lack the continuity and well-defined contour of cardiac dermatomes Such dermatomic patterns indicate that the autonomic nerves associated with cardiac pain have not been involved and that the patient is complaining of manifestations which have no relation to autonomic pathways or functions The preoccupation of the patient may be largely or entirely with his cardiac pain and its radiation If he possesses accurate knowledge of the anatomy and physiology of referred cardiac pain he may mimic anginal pain, referring it into dermatomes indistinguishable from those associated with anginal reference This may occur when the patient happens to be a physician or nurse or even an untutored layman who may have acquired in

formation by alert observation of anginal sufferers General or cardiac manifestations of autonomic activity may be present or absent

The following three examples of a cardiac conversion symptom illustrate in the first case the absence and in the other two cases the association of autonomic manifestations

Cardiac conversion symptom with bizarre dermatomic reference no autonomic manifestations

J B a man of 39 had had over a period of several years recurrent attacks of terrific pain in the heart and in the left precordium After some of these attacks he suffered from tightness in the chest for days at other times he developed pain in the head and a feeling of weakness and faintness. For the greater part of his adult life he was depressed fearful and anxious and found it extremely hard to have pleasant relations with his close relatives or most business colleagues He had two unsuccessful marriages a son now 15 was born of the first marriage The son and the patient s parents were a constant source of distress even when he so much as thought of meeting them The depression and withdrawal behavior grew steadily worse and he spent a considerable part of four successive years in several mental institutions undergoing treatment by insulin metrazol and electric shock his left arm was fractured under metrazol therapy

An outstanding and recurrent complaint was severe precordial pain radiating often into the left dermatomic area supplied by the Th 1 to 6 nerves The dermatomic reference consisted of irregular and disconnected portions or islands of the skin of the left forearm Pain was frequently set off by acute emotional distress but occasionally without discernible provocation Organic heart disease and autonomic features such as tachycardia vasomotor manifestations, sweating elevation in blood pressure etc were absent An especially interesting feature was his description of the occasional paradoxical onset of heart pain when he was apparently calm and not under intense emotional strain

Under renewed psychotherapy he was eventually able to establish a closer and better relationship with his parents and his son he extricated himself from a tormenting friendship with a girlfriend and though he still retained obsessional and some hallucinatory symptoms his general adjustment improved The cardiac manifestations grew less frequent and milder

Cardiac conversion symptom associated with autonomic manifestations

F R an intelligent woman of 55 apparently not self indulgent the mother of two young adult children had married at the age of 0 a man of foreign extraction 25 years older than herself Shortly after the marriage she realized that the husband was emotionally difficult and that his intellectual interests and family background were very different from her own For more than 20 years she had frequent attacks of cardiac pain often with radiation up the sternum and into the left arm These attacks were nearly always associated with marked vasomotor flushes axillary sweating cold moist hands rapid pulse a feeling of goneness and a sensation of choking She was obliged to spend several days or weeks in bed and her prostration was marked by these episodes Her symptoms had been ascribed to metabolic disease endocrinal disturbance and at one time to acute coronary occlusion with myocardial infarction

Physical examination revealed no organic heart disease The flushing she described was witnessed and proved to be of a striking violaceous hue involving large areas of the skin It lasted about 15 to 20 minutes during an attack and then gave place to a mild copper like color which persisted for hours edema of the skin or throat was never a feature

It took but little delving to establish that the patient had been trying to do her best to

keep up her marriage with a man whom she respected but who was still alien in many respects and inadequate to her emotional and sexual needs She had neither the courage nor the conscious wish to protest aloud but protest she did by means of her conversion symptom i e through the heart The attacks of cardiac pain which seemed to simulate anginal pain and were associated with autonomic reactions became less frequent and less marked when she succeeded in finding work and interests to keep her away from home most of the week

Cardiac conversion symptom associated with autonomic manifestations

G S a young man of 23 who had had an agitated and stormy childhood and adolescence began at the age of 10 to have attacks of severe palpitation and pain in the heart which travelled into the left upper arm Practically always these attacks were accompanied by sweating and clammy hands blushing and a sensation of feeling hot Organic heart disease was excluded

Persistent questioning revealed that the attacks had come on originally when he was 10 years old and passed through severe anxiety and panic on discovering that his parents were about to break up the home The parents however remained together for the next 12 years but during this period the threat of their separating never quite left him They were finally divorced when he was 22 but the cardiac and other symptoms persisted for two years before he was subjected to psychotherapy With psychotherapeutic guidance the basis of his worry became clear to him and as his confidence in his own worth and personality grew stronger his symptoms became less severe

The autonomic manifestations which probably included the element of pain were associated in this case with long continued emotional tension induced in childhood

4 *Malingered and referred heart pain* The malingerer has a clear, calculated aim and no inner load or pressure that requires lifting pain in the heart serves his realistic goal If unskilled or ignorant in the ways of cardiac pain he is likely to refer the pain into dermatomes that are irregular and unorthodox, or his information and the ensuing mimicry may be accurate The malingerer will seldom exhibit signs of autonomic mass reaction Character defects and antisocial thinking are not instigators of autonomic hyperactivity

Cardiac pain and referred cardiac pain as a malingered manifestation

A 40 year old female E G always in good health developed for a period of a year episodes of severe pain in the left chest which radiated up the sternum into the left neck and down the left arm The attacks were usually accompanied by a choking sensation Walking or climbing stairs appeared to bring on the attacks The pain was referred accurately along the ulnar distribution of the left forearm and according to her description involved the entire little finger but only the ulnar side of the fourth finger She was very tender to pressure over the anterior left 5th to 7th ribs

Organic heart disease was readily excluded and yet her symptoms persisted despite strong reassurance by competent physicians that she had no heart disease and therefore no ground for worry After a few interviews it became evident that the patient was greatly disturbed over the infidelity of her husband and suffered intensely from jealousy and anxiety which were more marked during the three to four nights a week she was left alone at home The history disclosed also that a much older brother had had attacks of acute coronary occlusion associated with pain and distribution of pain almost identical with her own She recalled too that walking gave her brother pain in the heart and in the left arm

She was an intelligent straightforward woman and readily admitted that she had knowingly taken on her symptoms to frighten her husband and keep him from wandering She

wanted to prove to or souse worry in her husband s mind about her health and she knew all along he was not sick and was amazed that the specialists had had to make so many tests to reach the same conclusion She was advised to try to save her marriage with her head and not with heart symptoms.

This is an example of malingering free of autonomic manifestations. The pain and its reference accurately followed the ulnar distribution she had witnessed in connection with her brother s cardiac illness

Manifestations in Subjects with Cardiovascular Disease

The subject with organic heart disease suffers as far as emotions go from a double disadvantage Emotional stimuli or stress may affect the organic disease or the latter already associated with physical and emotional suffering may give rise to emotional reactions Case R J R (p 31) is a demonstration of superadded grave heart damage terminating in death induced by grief and examples are frequent of patients with organic heart disease who develop anxiety and even panic at the thought of a recurrent attack of heart illness

A sensible awareness of the likelihood of the recurrence or aggravation of heart disease should be part of the patient s equipment Yet although these dangers in many instances may be slight and practically nonexistent emotional disturbances accompanied by cardiac complaints may be marked This is usually accounted for by the fact that the patient having lived through the dread and anguish of a previous cardiac illness and almost touched death, is conditioned to react in terms of his experience with his sick cardiac apparatus It may take but a minor event such as a rapid pulse, mild palpitation, or a short pang of pain in the heart region to produce great emotional stress The panic and the physiological events which accompany it are quickly provoked because they are so to speak close to the heart Furthermore many subjects with organic heart disease are psychoneurotic and in them the readiness to react emotionally and the exaggerated nature of the reaction point to an underlying emotional maladjustment

As a general rule emotional stimuli in patients with organic heart disease produce some degree of autonomic hyperactivity even when the cardiac apparatus undergoes no further physiologic change or increased morphologic damage General ed sweating, salivation rise in blood pressure tachycardia increased respiration gastrointestinal symptoms disturbances in sleep and even fever are not rare These features of an autonomic mass reaction are not necessarily evidence of fresh organic disease Emotional stimuli may give rise to an autonomic mass reaction independent of an existing organic heart disease or they may affect the already damaged cardiac apparatus causing superadded attacks of angina pectoris or acute myocardial infarction the latter in turn producing autonomic hyperactivity In either event the general autonomic and cardiac manifestations are apt to be more marked than in individuals free of organic disease

Organic heart disease associated with coronary sclerosis, hypertension, myo cardial infarction is often responsible for anginal pain with reference into well defined cardiac dermatomes, and this is true whether the pain is brought on by exertion or other precipitating elements including emotional strain The organic cardiac state, on the other hand, may appear to be little affected by emotional factors and go on to serious symptoms and death This is illustrated by the case of a comparatively young man who suddenly succumbed to or ganic heart disease following a period of ten weeks of striking improvement of his emotional strain and conflicts

Organic heart disease and emotional conflict

S L a man of 45 in good health and a fine athlete complained that for several months he had had repeated attacks of pain in the left chest transmitted into the left arm The pain first appeared when he was 36 years old recurred three years later and again about ten weeks before his terminal illness He was a heavy cigarette smoker drank infrequent but large amounts of alcohol and was very vigorous in all his physical activities Despite the absence of structural heart disease the pain was looked upon as anginal because the patient was clearly not a malingerer he had an unmistakable effort syndrome and his pain was referred into well defined cardiac dermatomes

As far back as he could remember he was under the influence of a strong and gifted older brother and he recalled vividly that at the age of six he was humiliated at the protection this brother manifested by separating him in a fight from an opponent who was getting the worst of it The patient referred to this incident many times All through his early youth he experi enced anguish and self reproach at being a meek male trying to follow in his brother s foot steps He had married against his will and his wife s wealth made everything easy for him but robbed him of his manhood even though he was an adequate male sexually He was forever vacillating between complying with his brother s and his wife s wishes and striking out for himself

He improved rather rapidly under psychotherapy commenced looking after his business affairs methodically and established a quieter and warmer companionship with his wife and two children He began to enjoy what he called the best and happiest days of his life and was apparently free of anxiety and depression About ten weeks after the start of the improve ment he was suddenly stricken with an acute attack of coronary occlusion and myocardial infarction and died within a few days The alleviation of his long standing emotional conflict and strain failed to prevent the terminal acute coronary attack

An individual with organic heart disease is also subject to the occurrence of nonanginal pain This form of pain will develop by mechanisms practically identical with those described in the nonorganic group Simulations of cardiac pain produced by noncardiac lesions are not rare and add difficulty and con fusion to the problems of diagnosis and therapy Mimicry and malingering of anginal pain also occur in this group of patients The nonanginal forms of pain are possibly conjured up more readily because the patient retains the memory of having lived through the reactions and manifestations that accompany organic heart disease The following case illustrates the concurrence of anginal pain due to organic heart disease and of pain which simulated the anginal type The latter was associated with a psychological mechanism manifested in early childhood

Organic heart disease with anginal and simulated cardiac pain

A 64 year old male A R sustained at the age of 60 an acute coronary occlusion accompanied by massive heart muscle infarction he had marked arterial hypertension for 15 years previously After a severe illness of several weeks he became a chronic invalid with congestive heart failure passing through three critical attacks of acute left ventricular failure brought on by emotional provocation The physical examination at the age of 64 revealed a heart greatly enlarged notably the left ventricle the electrocardiogram showed signs of chronic myocardial damage and evidence of an old anterior wall infarction Emotional excitement often produced severe anginal pain with characteristic dermatomic radiation At other times, especially when balked by his adult son he complained of pain in his heart region that seemed to be hysterical

For at least the latter 30 years of his adult life he was a high strung aggressive person determined to succeed and in his own way As a child and young adolescent he would have attacks of pain in his heart and have to lie down Many of these attacks were precipitated by altercations with his parents later with his wife or children and he recalled that even as a youn child he was likely to experience pain in the heart region when he failed to have his own wa

Summary

The autonomic mass action and the radiation of pain into dermatomes are important elements in the study of psychosomatic disorders

The psychosomatic disorders related to the heart may be divided into two groups one concerns subjects who have a normal cardiovascular system the other subjects with organic heart disease In the former group emotional disturbances will produce systemic autonomic manifestations that are usually mild and cardiac features which are for the most part subjective and prominent The cardiac pain will seldom conform to the pattern of anginal pain and its dermatomic reference The pain may serve as a conversion symptom or even take on fantasy or hallucinatory features or it may be cleverly simulated or malingered making the differentiation from anginal pain sometimes extremely difficult

The group with organic heart disease exhibits the same tendency to systemic autonomic as well as cardiac manifestations These may all conform to the clinical responses previously experienced as the result of the organic disease, or cardiac pain may be superimposed as a simulated malingered or conversion manifestation which remains outside the realm and functions of the autonomic nervous system Emotional factors can however precipitate new damage to the cardiovascular apparatus

BIBLIOGRAPHY

The following references were consulted in the preparation of this chapter

ALEXANDER F Functional disturbances of psychogenic origin J A M A 1933 *100* 469

— Fundamental concepts of psychosomatic research Psychogenesis conversion specificity Psychosomatic Med 1943 *5* 205

— BACON C LEVEY H LEVINE M AND WILSON G The influence of psychogenic factors upon gastrointestinal disturbances a symposium A report on research carried on at the Chicago Institute for Psychoanalysis Psychoanal Quart 1934 *3* 501

— AND FRENCH T M Studies in Psychosomatic Medicine New York The Ronald Press 1948

—— AND MENNINGER W C The relation of persecutory delusions to the functioning of the gastrointestinal tract J Nerv & Mental Dis 1936 *84* 541
BARD P Central nervous mechanisms for emotional patterns in animals Research Pbl A Nerv & Ment Dis 1939 *19* 100
——, AND MOUNTCASTLE, V B Some forebrain mechanisms involved in expression of rage with special reference to suppression of angry behavior The frontal lobes Research Pbl A Nerv & Ment Dis 1947 *27* 362
CANNON W B Bodily Changes in Pain Hunger Fear and Rage New York D Appleton Century Co 1934
DEUTSCH F Biologie und Physiologie der Krankheitsgenese Int Z Psychoanal 1922 *8* 290
DRAPER G AND TOURAINE, G A The man environment unit and peptic ulcer Arch Int Med 1932 *49* 616
DUNBAR H F Emotions and bodily changes 2nd ed New York Columbia Univ Press 1938
—— WOLFE T AND RIOCH N The psychic component of the disease process in cardiac diabetic and fracture patients Am J Psychiat 1939 *93* 649
FENICHEL O The psychoanalytic theory of neurosis New York Wm Norton 1945
FERENCZI, S The phenomena of hysterical materialization In Further Contributions to the Theory and Technique of Psychoanalysis London The Hogarth Press 1926
FREUD S Collected Papers Vols I–IV London The Hogarth Press 1948
GUNTHER L AND MENNINGER K A Intermittent extrasystole directly associated with emotional conflict a case report Bull Menninger Clinic 1939 *3* 164
KLUVER H AND BUCY P C Preliminary analysis of functions of the temporal lobes in monkeys Arch Neurol & Psychiat Chicago 1939 *42* 979
MENNINGER K A AND MENNINGER W C Psychoanalytic observations in cardiac disorders Am Heart J 1936 *11* 10
MILLER H K Central Autonomic Regulations in Health and Disease New York Grune & Stratton 1942
—— AND SPIEGEL E A Sleep induced by subthalamic lesions with the hypothalamus intact Proc Soc Exper Biol & Med 1940 *43* 300
MILLER M L AND McLEAN H V The status of the emotions in palpitation and extrasystoles with a note on the effort syndrome Psychoanal Quart 1941 *10* 545
RANSON H W The hypothalamus its significance for visceral innervation and emotional expression Tr Coll Phys Phila 1934 *2* 222 (4th series)
SPIEGEL E A MILLER H K AND OPPENHEIMER M J Efferent forebrain systems involved in the production of rage reactions after decortication Am J Physiol 1940 *129* 470 Also in J Neurophysiol 1940 *3* 538
WEISS E AND ENGLISH O S Psychosomatic Medicine Philadelphia W B Saunders Co, 1943
WILSON G W Acute laryngitis a conversion symptom Psychoanal Rev 1934 *21* 408
WOLFE T P Emotions and organic heart disease Am J Psychiat 1936 *93* 681
WOODWORTH R S AND SHERRINGTON C S A pseudoaffective reflex and its spinal path J Physiol 1904 *31* 234

SECTION SEVEN

Treatment of Angina Pectoris and Myocardial Infarction

CHAPTER XXI

General Management and Medical Treatment

Introduction

This chapter is divided into two parts The first is concerned with the acute episodes of coronary insufficiency acute myocardial infarction with or without acute coronary occlusion and the complications and sequelae at the time of the acute episode or shortly thereafter The second part deals with the interval state between recurrent episodes and the eventual chronic state of the patient Understanding the symptoms and signs of each condition in relation to the activities of the autonomic nervous apparatus will we believe bring the medical and surgical therapy into better focus and give the physician a deeper insight into the genesis and mechanisms of the clinical features and a sharper skill with which to treat them

Part I Acute Episodes

A Treatment of Acute Coronary Insufficiency (Angina Pectoris)

For most cases of acute coronary insufficiency even if general systemic manifestations are marked it will suffice to put the patient to bed for approximately a week remove him from physical and other influences which favor or precipitate an attack administer some form of sedation and not less important rebuild his confidence and hope He must be guarded against what is for him an excessive cardiac demand in the face of his impaired or tired coronary circulation and he must be protected from local or systemic causes which damage the heart This may mean guarding against undue exertion or exposure to cold and wind avoiding overweight especially in diabetics and hypertensive individuals interdicting large meals or eating before retiring re-educating the individual to avoid wasteful loss of energy or upsetting his emotional balance as in fancied or even well founded anxieties Smoking often should be banned with finality The danger of a coronary reflex from an extracardiac condition such as a diseased gall bladder duodenal ulcer or esophageal herniation should be removed by treating these conditions Anemia or hyperthyroidism of par

oxysmal tachycardia, any of which may induce coronary insufficiency, must be corrected The general autonomic disturbance is usually not severe and central effects such as fever, leukocytosis, etc, are absent or slight

The patient may require first and almost foremost *immediate relief of his pain* This is best accomplished by giving nitroglycerin* 0 0003 to 0 0006 (gr $\frac{1}{200}$ to $\frac{1}{100}$) sublingually or orally, the preparation can be repeated frequently The other nitrite products are not as good Alcohol is often an excellent coronary dilator, 30 to 60 cc (1 to 2 ounces) is enough, given "straight" and at frequent intervals Papaverine, proposed by Pal[30] many years ago and recently raised to popularity in this country, is a good coronary dilator Doses of 0 06 to 0 24 (gr 1 to 4) three to four times a day are given by mouth or intravenously *Nicotinic acid, 50 to 100 mg daily, has been advocated as an effective means* of increasing collateral circulation The best recourse in many cases is morphine given without delay and in adequate amounts, 0 015 to 0 030 (gr $\frac{1}{4}$ to $\frac{1}{2}$) This can be followed by a good morphine derivative or substitute (p 274) For poor or restless sleep, barbiturates are often helpful carbrital 0 3 to 0 6 (gr 5 to 10), nembutal 0 1 to 0 2 (gr $1\frac{1}{2}$ to 3), seconal 0 1 to 0 2 (gr $1\frac{1}{2}$ to 3), are good preparations Except for the use of nitroglycerin as in acute coronary insufficiency, these directions are also applicable to acute myocardial infarction with or without acute coronary occlusion

B Treatment of Acute Myocardial Infarction with or without Acute Coronary Occlusion

General Considerations

Although the autonomic mass action associated with acute myocardial infarction is more vigorous than in the uncomplicated episode of acute coronary insufficiency many of the central autonomic manifestations frequently require no direct or special attention, provided the cardiovascular apparatus holds its own and is spared repeated or overwhelming injury Thus fever, leukocytosis, abnormal sedimentation rate, sleep disturbances and mild or moderate changes in water balance subside or right themselves after the storm of an attack lets up When, however the cardiovascular features are marked or critical, it becomes imperative to determine whether *the myocardium has suffered* as a result of acute coronary occlusion or whether the injury has been produced by severe hemorrhage, postoperative shock etc and is unattended by acute coronary occlusion In the latter instance measures such as transfusion of blood, vigorous antishock therapy, etc are obligatory and can be life saving whereas such measures may be contraindicated in the former case

In any event, it is not wise to move the patient in the throes of an attack

* Recent studies in the dog have raised the theoretical question may not nitroglycerin actually increase the work of *the heart when this organ is already damaged?* (Wegria[36]) *and* this may apply to other vasodilators such as papaverine

The victim himself instinctively becomes immobile and this clue the intelligent physician recognizes and follows The physician will therefore carry out two imperative rules *immediately* first for the time being do not move or disturb the patient and second give morphine freely and enough to put him to sleep The observance of these rules may mean the difference between life and death for the most painstaking and careful handling of the patient to move or transport him for even a very short distance may be fatal in the case of acute coronary occlusion leading to fresh *occlusion—extension of the occlusion or the* spreading of heart muscle damage Withholding the morphine is no less dangerous Violent pain shock and mental anguish are pronounced and all effort must be made to help the victim survive The best and first recourse is to induce sleep at once and keep the patient undisturbed while asleep The morphine is administered hypodermically 0 015 (gr $\frac{1}{4}$) sometimes with atropine sulphate 0 0004 (gr $\frac{1}{150}$) It is very important not to wait too long for a next dose with or without atropine ten to fifteen minutes are enough or the double quantity may be required at the onset There are cases that require subsequent doses totaling 0 06 (gr 1) or more within an hour or less time After having given the first 0 03 (gr $\frac{1}{2}$) subsequent dosage may be effective in units of 0 015 (gr $\frac{1}{4}$) or 0 0075 (gr $\frac{1}{8}$) Nitroglycerin is seldom if ever of value The *patient* is kept warm covered with light weight woolen blankets especially in the *cold* season of the year the ventilation of the room suitably adjusted and *visitors* and all family members excluded It is not necessary to urge food or water upon the patient until he has had time to benefit from the morphine *The greatest* part of wisdom at this stage is to do as little as possible and sit tight Even the relief of a full bladder a full rectum meteorism are deferred if at all possible until the pain and shock subside

Mental State

Although *not often* the case the mental and emotional aspects of an attack not pain may dominate the scene all too often they play a neglected but important part in the outcome of the patient A premonitory stage or aura may precede shock or severe pain Mental anguish *may* be very intense during the attack and possesses characteristics that almost *seem* to be pathognomonic Of this the attending physician must be aware the *moment* he meets his patient Morphine is given with no loss *of time* and the sufferer is secluded and kept quiet Before the drug dulls the mind *the patient* will be terrorized and certain that death is near to overtake him in a very few minutes He will be alert to every play of *expression* on the features *of those around* him and he will catch almost imperceptible gestures or inflections of the voice that will mean to him encouragement and *hope or confirmation* of his worst fears The quiet and firmness with which the physician *conducts himself* the absence of visible signs of apprehension in his *manner* the buoyancy and resoluteness with which

he takes hold of the case, are strong props for the patient. This calming attitude helps change the patient from a panic stricken and helpless object to a willing and cooperative subject and in this state the effectiveness of morphine is enhanced.

Following the sleep and rest of the first hours the physician will again have an opportunity to instill hope and confidence. He is now in a position to emphasize, in as few words as posssible, that the patient has passed the violence of the storm and, to continue the figure of speech, the patient like a ship will need care and skillful guidance before reaching calm waters. After this, generally speaking, the less the physician says by way of bolstering up the courage of the patient, the better. There are too many unpredictable dangers ahead. It is inadvisable therefore to appear too sanguine. To say nothing and thus avoid opening up doubts and apprehensions in the mind of the patient is good practice.

Pain

The physician may be conscious of the danger of shock and the menace of heart failure but the intense pain of acute myocardial infarction, intensified perhaps by a concurrent acute coronary occlusion, is his immediate concern. Pain ceases appreciably after its early fury but it can grow more severe or it can linger sharp and strong for a long time and then stop abruptly or wane before stopping. The pain may recur in waves or spasms, and as intense or devastating as the initial attack. Fresh pain, and as bad as the original agony, may be due to a new acute coronary occlusion with infarction of a fresh myocardial area or to extension of the original coronary thrombus, or to pericardial involvement.

The best means for subduing the pain, in addition to complete rest, are morphine and oxygen. The rest must be complete and absolute. The morphine should be used liberally, or a morphine substitute: *codeine sulphate* 0.03 to 0.06 (gr $\frac{1}{2}$ to 1), demerol 50 to 100 mg., dilaudid 0.002 to 0.004 (gr $\frac{1}{32}$ to $\frac{1}{16}$), *pantopon* 0.01 *to* 0.02 (*gr* $\frac{1}{6}$ *to* $\frac{1}{3}$), *papaverine hydrochloride* 0.06 to 0.24 (gr 1 to 4). Sometimes it is well to give barbiturates alone or supplemented by drugs of the morphine group. The barbiturates have advantages over the morphine group: they produce few if any of the morphine "after effects", sleep is not as heavy, the respirations escape the danger of depression, the bowel and bladder functions are not interfered with and, of course, habituation is less of a problem. These drugs are however not free of disadvantages. They are sometimes capricious in their action leaving "after sleep" symptoms, depression or excitement, and are known to cause alarming anaphylactic shock symptoms, and occasionally when sorely needed fail to bring sleep. The following preparations are in general use: adalin 0.6 to 1.2 (gr. 10 to 20), allonal 0.25 to 0.5

(gr 4 to 8) amytal 0 1 to 0.3 (gr 1½ to 4½), amytal sodium 0 1 to 0.3 (gr 1½ to 4½) carbrital 0.3 to 0 6 (gr 5 to 10) dial 0 1 to 0 3 (gr 1½ to 4½) nembutal 0 1 to 0 2 (gr 1½ to 3), phanodorn 0 1 to 0 2 (gr 1½ to 3), seconal 0 1 to 0 2 (gr 1½ to 3) A very useful product for subcutaneous administration is sodium luminal put up in sterile ampules the dose is 0 12 to 0 24 (gr 2 to 4) every four to eight hours Some patients need mild but uninterrupted sedation for several weeks after the acute paroxysm This is best accomplished with bromides phenobarbital or codeine

The prompt subduing of pain helps minimize shock and may even aid in preventing reflex coronary vasoconstriction This constriction probably vagal in nature is sometimes relieved by atropine 0 0005 to 0 001 (gr $\frac{1}{120}$ to $\frac{1}{60}$) given every four hours for several doses The administration of papaverine as early as possible is recommended to overcome vasoconstriction, and since according to McEachern et al[23] and Lindner and Katz[11] the drug appears to have an antifibrillation effect in dogs it may have similar value in man In the dog experimental coronary ligature with acute myocardial infarction seems to favor reflex coronary constriction This chain of events is conducive to the onset of ventricular fibrillation (LeRoy and Snider[10]) A similar danger probably exists in man The occurrence of reflex vagal constriction allegedly exerted on the uninvolved portion of the coronary circulation when a coronary vessel is acutely occluded is questioned in some quarters

No time should be lost in giving oxygen therapy for the relief of pain While the patient is still under the influence of morphine and as soon as he has been transported to a bed an oxygen tent should be placed over him The usual equipment for tent treatment consists of motor-driven apparatus The concentration of oxygen is maintained at 40 to 60 per cent and to insure this concentration frequent testing of the atmospheric content of the tent is necessary the temperature of the tent is kept at about 60 F The patient remains in the tent as many days as necessary until the peril of heart failure is over It is better not to remove him prematurely but rather to err on the safe side by allowing him to remain there an extra day or so The tent must be lifted off only in the presence of a physician because of grave danger that the patient may unexpectedly collapse it should be kept in readiness for an additional day or two in case of emergency

Other methods of administering oxygen are sometimes better tolerated but are in general less effective The nasal catheter method is fairly good and provides almost 40 per cent of oxygen if the catheters are properly adjusted in the nostrils As a rule the patient develops irritation and dryness in the throat and a troublesome dry cough and even the frequent sprayings with mild anesthetics will not permit its use beyond a comparatively short time Several face masks are in popular use and in many cases quite satisfactory The method of administering oxygen under high pressure developed by the United States Army

possesses advantages at least from a physiological point of view, but clinical information on its use in myocardial infarction is not general

All nursing and this must be of the most skillful order, is performed with the patient in the tent He should be propped up at an angle of 30 or 40 degrees, this also keeps the tongue from falling back He is spared every movement, however slight, in the beginning fluids are given with a medicine dropper or teaspoon

Shock

Oxygen therapy and the relief of pain are powerful agents in combating shock In addition, the patient should be kept warm although on this point there has been recent discussion as to whether keeping the patient cool rather than warm is not a better way of treating shock Cardiac stimulants may be dangerous and are perhaps better withheld unless the heart action is failing so rapidly that little additional risk is involved in active stimulation In the presence of rapidly developing or developed acute heart failure, caffeine sodium benzoate is injected 0 12 to 0 5 (gr 2 to $7\frac{1}{2}$) subcutaneously, intramuscularly or even intravenously The following may also be used adrenalin 1 1000 *solution 0 3 to 1 0 (M 5 to 10) or for slower and more continuous absorption* adrenalin in oil [4] 0 75 to 1 5 cc (1 5 to 3 mg) subcutaneously every four hours in the same dosage, or ephedrine 0 0225 to 0 030 (gr $\frac{3}{8}$ to $\frac{1}{2}$) by mouth these products are to be given with great caution in the cardiac states under consideration The intravenous use of ouabain or strophanthin digitalis or aminophyllin may be dramatically life saving For the sake of convenience these three drugs are discussed rather fully at this juncture

Digitalis The administration of digitalis bodies may *be very effective when* the circulation is failing Acute heart failure under almost all circumstances, is a prime indication for digitalis the cardiac rhythm is not necessarily a determinant [7] If time permits it is best to give the drug by mouth and not too rapidly, in divided doses within 12 to 24 hours or when haste is essential as a full initial dose

A number of dry leaf products prepared by reliable pharmaceutical firms are good *for oral use It is not necessary to adhere to the method of cat unit* dosage Preparations are administered at the rate of about 0 01 (gr $\frac{1}{60}$) of dry drug per pound of body weight A man weighing 150 pounds will therefore receive about $22\frac{1}{2}$ grains Slowing of the ventricular rate to within the normal range is a sign that digitalization has been accomplished The maintenance dose is gr 1 to 2 of dry substance Digitaline (Nativelle) the original digitoxin a pure crystalline product well known on the continent for many decades has been brought *into popular use in this country through the studies of* Gold and his associates [15] Rapid digitalization is achieved by giving 1 2 mg as one dose or in two or three divided doses at about three hour intervals the maintenance

dose is between 0 1 and 0 2 mg daily The drug is completely absorbed has a rapid action and is practically free of untoward gastric effects Digitalis intoxication with it may be insidious and rather severe

The intravenous use of digitalis bodies is an excellent procedure in many cases Good preparations are available With digilolin (Ciba) full digitalization is induced by 6 cc per 100 pounds of body weight given perhaps in two or three doses at two to four hour intervals in a cardiac emergency, 4 cc may be introduced Digitalization is reached with about 6 to 8 cc of cedilanid lanatoside C (Sandoz) as a single dose or divided over 12 to 24 hours

The intravenous use of calcium-containing preparations is best omitted while the patient is taking digitalis The possible synergistic action of the drugs is not fully proved but cases of sudden death have been reported from intravenous injection of calcium salts in digitalized patients The combined use of ephedrine and digitalis is supposed to be more toxic than when either substance is used singly Ephedrine is therefore to be used very cautiously in digitalized subjects A caution about the use of quinidine with digitalis appears to be unduly stressed

Toxic effects of digitalis should be avoided disturbances in cardiac rhythm loss of appetite nausea and vomiting headache fatigue and drowsiness, disturbances in vision and skin rashes etc A disadvantage recently described in the use of digitalis or allied preparations is their propensity to shorten the coagulation time and thus produce thrombus formation

Ouabain The administration of ouabain or strophanthin is extremely valuable and sometimes the first choice The beneficial effect is obtained in minutes rather than in hours Oral administration is of little value intravenous injection highly effective The initial dose should be small at the very most 0 5 mg more usually 0 25 mg or half this amount A dose of 0 1 mg may be repeated every hour but not more than 1 mg of the glycoside is to be given in 24 hours It is sometimes preferable to distribute the single milligram in evenly divided doses spaced at 4 to 6 hour interval At the end of the emergency (it may last several days) digitalis is resorted to and maintained Although it is advisable to withhold these drugs until the patient is rid of digitalis bodies allowing two weeks at least for this purpose ouabain and strophanthin have been given with good results by experienced observers to patients who still had digitalis Monographs on ouabain strophanthin have been published by Fraenkel[10] Kisch[13]

Aminophyllin The intravenous use of aminophyllin when heart failure is an element in the shock has a sound physiologic basis (Howarth et al[11]) It is given very slowly and with full realization that sudden exitus has been ascribed to its intravenous use A stop watch is employed to insure slow injection The dose is 10 cc containing 0 24 Gm repeated every 6 to 8 hours and at shorter intervals if necessary during a critical state The intravenous use of the drug

may be replaced by rectal administration (p 285) Oral products have not been satisfactory Recently, glytheonate (p 285) has been recommended for this purpose

A useful procedure in some cases is the application of a tourniquet around each limb close to the torso The tourniquets are removed slowly and one at a time as soon as the feeble pulse grows stronger, within five to ten minutes in any event, and reapplied if necessary Intravenous injection of saline or glucose solutions and other products is best avoided if the heart is struggling against imminent failure

Cardiovascular Manifestations

These are always of primary significance During the acute attack the manifestations may be mild or severe, and this is usually conditioned by the force of the general autonomic upheaval and the character of the injury sustained by the cardiovascular system

Cardiac Arrhythmias Cardiac irregularities are not unusual They can come at once or early in the acute attack or appear in the early days thereafter or even later Their management and treatment require skill and experience Cardiac irregularities are produced by central autonomic effects or by changes in the peripheral cardiac innervations or by morphologic change in cardiac pace maker areas or the intracardiac conduction system

Paroxysmal Auricular Tachycardia Although in many circumstances of no grave import and often ending abruptly and spontaneously, this complication may be the precursor of auricular fibrillation, especially in the presence of acute infarction of heart muscle It is likely to yield spontaneously or upon carotid sinus pressure or pressure over the eyeball, or the induction of nausea and retching Mecholin used guardedly is useful about 25 and up to 40 mg given subcutaneously depending on the age of the patient it is never to be used intravenously oral use (50 to 100 mg) is not very effective

Paroxysmal Auricular Fibrillation This a serious complication, may disappear spontaneously within a few hours or days If it persists, it requires attention without delay Digitalis and quinidine are the indicated remedies Some cardiologists favor one drug as against the other, or prefer the prior use of one to the other We feel there is no fast rule and no practical contraindication to utilize one drug before the other Digitalization must be carried out with reasonable dispatch administering enough to come close to slowing the ventricles, digitalization is maintained by a suitable daily amount

Quinidine may be required after digitalization proves of no avail or quinidine may be the drug of first choice Quinidine sulphate 0 06 to 0 12 (gr 1 to 2) is given for two or three doses about 4 hours apart and if no untoward effect ensues, the drug is pushed more rapidly and in larger quantities 0 12 to 0 18 (gr 2 to 3) every three or two hours About 1 8 to 2 4 (gr 30 to 40) is given the

first day double this amount the following day 3 6 to 4 8 (gr 60 to 80) or more the next day and then perhaps tapered off We have had to give as much as 0 6 (gr 10) every hour for eighteen or twenty consecutive doses to restore sinus rhythm There are toxic dangers to bear in mind amblyopia severe skin rashes (purpura) depressive mental states etc , and its employment is contra indicated in renal disease thrombus formation in the heart and if strong sensi bility to the drug exists The prophylactic value of quinidine is not established

Certler and Yohalem[14] have used atabrine as a substitute for quinidine to arrest auricular fibrillation and supraventricular tachycardia Normal rhythm was promptly restored by a single dose of 0 6 Gm in 10 cc of 1 per cent nova caine administered intramuscularly and almost immediately by 0 1 Gm given intravenously The drug is not in general use and its usefulness and contra indication not yet established Its indiscriminate use is dangerous

Paroxysmal Auricular Flutter The tendency to spontaneous recovery and the indications for treatment are the same as for fibrillation Digitalization should not be prolonged for fear of inducing a permanent state of auricular fibrillation But this is a minor problem auricular fibrillation is a less harmful condition for the heart than uncontrolled and rapid flutter The flutter is sometimes stopped abruptly by exerting unilateral firm manual pressure over the vagus trunk in the neck o over the carotid sinus or upon an eyeball The induction of nausea and retching occasionally has a similar effect

Paroxysmal Ventricular Extrasystoles These are seen after acute myocardial infarction They should not be taken lightly because they can be the forerunner of ventricular fibrillation Quinidine given early is effective It is administered as already described (p 2,8) A preventive dose of 0 06 to 0 2 (gr 1 to 3) is supposed to be beneficial

Paroxysmal Ventricular Tachycardia This infrequent complication carries with it the danger of heart failure The prompt administration of quinidine is sometimes life-saving in warding off ventricular fibrillation and almost certain death Large doses may be necessary even as much as 0 6 to 1 2 (gr 10 to 20) every one to two hours smaller amounts are often effective The danger of excessive dosage is a secondary consideration in this emergency

Heart Block This is a grave complication when the heart is acutely damaged In some cases however the heart block is transient disappearing within a few hours or days indicating that no permanent injury was sustained to the A V tissues no special therapy is necessary The heart block seen in chronic myocardial disease after coronary occlusion and almost always associated with Stokes-Adams episodes (Gallavardin[11] [1] and Schwartz[22]) is of a different significance Schwartz[22] Schwartz and Jezer[24] originally described two mechanisms standstill of the ventricles and ventricular fibrillation They claimed in stand still there was hope of righting the rhythm of the heart by the prompt use of epinephrine hydrochloride (1 to 1000 aqueous solution) 0 5 to 1 cc (M, to 15)

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vasodilators other than nitroglycerin has wide acceptance and papaverine and aminophylline are widely employed

Spastic Phenomena Some individuals develop spasm of blood vessels other than the coronary vessels before the onset of a frank anginal seizure or spastic changes intermittent claudications may follow an anginal attack and the latter indeed is sometimes considered a coronary localization of a general spastic disorder The occurrence of intermittent claudication in the limbs vascular crisis in the brain abdomen, pelvis should put one on guard that the coronary vessels may be similarly seized Claudications in any part of the body are good reason for continuing general treatment of the patient when it would otherwise have been stopped For these spastic reactions all active and passive exertion should be reduced and exposure to severe meteorological change avoided Atropine 0 0004 to 0 0006 (gr $\frac{1}{150}$ to $\frac{1}{100}$) may be prescribed or other antispasmodic belladenal 0 1 to 0 2 (gr $1\frac{1}{2}$ to 3) 3 to 4 times daily syntropan 0 1 to 0 2 (gr $1\frac{1}{2}$ to 3) or trasentine 0.05 to 0 15 (gr $1\frac{1}{4}$ to $2\frac{1}{2}$) every 4 to 6 hours Papaverine 0 06 to 0 24 (gr 1 to 4) given several times a day is a good antispasmodic and whiskey alone or combined with these drugs is helpful

Constrictions may also attack noncardiovascular structures i e the bronchial laryngeal or pharyngeal musculature or the muscles of the epigastric region Sensations of severe constriction can be experienced in any of these regions and for them except perhaps in the case of bronchial spasm nitroglycerin 0 0003 to 0 0006 (gr $\frac{1}{200}$ to $\frac{1}{100}$) is as strikingly helpful as in many instances of blood vessel spasm The drug is given as a tablet or in fluid form and need not necessarily be administered under the tongue The same dose may be repeated within a few minutes and even repeated again The existence of hypertension is not a contraindication The tablet form of the drug must be fresh it will keep if securely stopped to exclude air Amyl nitrite 0 2 cc is not as good a remedy nor are the other dilators of the nitrite group as effective except perhaps erythrol tetranitrite 0 03 to 0 06 (gr $\frac{1}{2}$ to 1) Papaverine seems to be quite effective and is given rather freely 0 06 to 0 24 (gr 1 to 4) about every 4 hours This may be combined with whiskey in 30 to 60 cc (ʒ1 to 2) doses several times a day For spasm of the bronchial musculature it may be necessary to give with caution small doses of aqueous adrenalin (1 1000) 0.3 to 0 6 cc notwithstanding the coronary nature of the underlying illness

Cardiovascular Complications

The major complications which appear during an acute cardiac attack shortly thereafter or during the chronic state are (1) fresh extension of acute myocardial damage (2) supervention of a fresh infarction with or without acute coronary thrombosis (3) reflex vagal constriction of the coronary circulation (4) acute pericarditis (5) acute embolization to the lungs (6) acute pulmonary edema especially in hypertensive patients in whom the left ventricle fails and (7) general anasarca

intramuscularly or even intravenously, repeating the dose every few hours and continuing it after restoration to normal sinus rhythm as a preventive The other mechanism associated with heart block is ventricular fibrillation and with this complication most cases terminate fatally within a few seconds or minutes However, there are patients who live through numerous episodes of ventricular fibrillation within the day and the night (Schwartz), and for them epinephrine is contraindicated Schwartz has now come to believe that the classification of Stokes Adams disease based on the two mechanisms he described may have to be modified

In ventricular standstill, ephedrine sulfate and barium chloride have been recommended The dose of ephedrine sulfate is 0 0225 to 0 030 (gr ⅜ to ½), it is not as effective as epinephrine Barium chloride is administered three or four times a day in amounts of 0 015 to 0 03 (gr ¼ to ½), the drug has no place as a prophylactic measure There is theoretical ground for withholding quinidine *in Stokes Adams attacks* because experimentally it tends to favor the onset of ventricular fibrillation

Blood Pressure Changes The low blood pressure which accompanies acute myocardial infarction is treated by the measures already described for the support of the circulation (p 276) A steady and maintained rise in blood pressure usually parallels the improvement in general condition Persistent low blood pressure, especially of the diastolic level, 50 mm Hg or less (assuming that aortic insufficiency is not a factor) is very serious In some special circumstances and with due recognition of the hazard to the damaged heart small doses of ephedrine by mouth every three or four hours or subcutaneously in an aqueous or oil vehicle are worth using, epinephrine in oil may also be used Since the heart may be *too severely maimed to tolerate sudden and forceful* activity, stimulation therapy, as with caffeine, should be employed with great circumspection Digitalis is of doubtful value though there are some authorities who recommend it in regular small 'tonic' doses Cortin or other adrenal cortex preparations such as desoxycorticosterone have been advocated, but their value in this condition is not established Large amounts of salt as recommended for hypotension and asthenia in Addison s disease is seldom advisable since congestive heart failure may prove to be a latent or even *full blown complication* The application of tourniquets mentioned in connection with the treatment of shock *is not indicated in states of hypotension that last days or weeks*

A sudden violent leap in blood pressure to 200 mm Hg systolic or more seen in a comparatively limited number of cases with the onset of an attack calls for no special treatment The blood pressure will generally drop within a few minutes to its previous level or close to it This abrupt elevation in blood pressure is not too rare in an anginal attack in hypertensive individuals Acute hypertension is infrequent in acute myocardial infarction The use of vasodilators such as nitroglycerin etc *is seldom effective in acute heart in*farction especially if complicated by acute coronary occlusion The use of

for several days even when the drug has been withdrawn The supervention of bleeding tendency or of a markedly lowered prothrombin level calls for the prompt use of blood transfusion and vitamin K The synthetic product of vitamin K (menadione) is highly recommended and 60 to 70 mg are administered and repeated as required Allen[1-3] claims that the guide for the use of dicumarol is not the prothrombin time but rather the prothrombin level i e the percentage of the normal He feels that the prothrombin time may change because of variation in potency of thromboplastins

Heparin and dicumarol are often used simultaneously For adults 50 mg of heparin are given intravenously every 4 hours during 36 to 48 hours With the first dose of heparin 300 mg of dicumarol are given by mouth and on the following day reduced to 200 mg Thereafter it may be sufficient to rely on dicumarol alone giving about 200 mg a day or less according to the prothrombin level A recent and full report on the use of these drugs in acute coronary occlusion has been published by Wright et al[40]

Contraindications to the use of anticoagulants are blood dyscrasias bleeding tendencies gastric or duodenal ulcer advanced liver or renal disease postoperative states especially after brain surgery A point worth remembering is that dicumarol makes the sedimentation test less dependable

(4) *Acute Pericarditis* This complication is noted in those forms of acute myocardial infarction which involve the pericardial surface of the heart It is in most cases a comparatively early complication and far more apt to occur with acute coronary occlusion where the injury to the heart extends to the pericardial lining Special treatment is seldom required An ice bag applied locally and sedation for pain are helpful Turning from side to side may cause pain and should be avoided The best therapy for this complication is careful attention to the underlying myocardial damage

(5) *Reflex (Vagal) Coronary Constriction* Although the problem of whether the coronary vessels in man actually undergo constriction is far from settled (Opdyke and Selkurt[29]) considerable evidence points in this direction Nitroglycerin is given at once under the tongue 0 000, (gr $\frac{1}{150}$) (p 242) and repeated if coronary spasm is suspected Other preparations are papaverine gr 1 to 4 several times a day atropine 0 0004 to 0 0006 (gr $\frac{1}{150}$ to $\frac{1}{100}$) and the frequent use of small amounts of whiskey Atropine is given either by mouth or subcutaneously limiting the total dose in twenty four hours to about 3 mg if tolerated The drug in smaller amounts may be repeated over several days as a preventive measure For constriction that recurs frequently or appears to be intractable aminophyllin may bring relief It is given intravenously and repeated every 6 to 8 hours as required It is sometimes of advantage to continue the aminophyllin several days longer than the atropine if anginal pain from reflex coronary constriction is stubborn or if breathing is irregular or of the Cheyne Stokes type or if cyanosis persists The efficacy of quinidine

(1) Extension of an acute myocardial damage (2) the supervention of a fresh infarction, and (3) acute pulmonary embolization require anticoagulant therapy in addition to the other measures already considered for each of the complications These complications are far from negligible, acute pulmonary embolization, for example, as a cause of death in acute myocardial infarction is about 10 per cent, according to Woods and Barnes[39] The anticoagulants are widely used and although indications and methods for employment are not finally established, the drugs appear to have a valuable place in therapy

The drugs are also indicated when venous clots in limbs or other locations are likely to become dislodged and threaten to embolize in the lungs or other organs Confinement to bed enhances this danger, the bedridden patient with acute myocardial injury may be in greater jeopardy from emboli loosened from his peripheral veins than from intracardiac thrombi Ligating the veins in the groin may be necessary and can be life saving Anticoagulants should be instituted without delay but very cautiously

The two anticoagulants employed are heparin and dicumarol (Allen et al,[1-3] Loewe) Heparin acts more promptly, the effect does not endure and can be stopped quickly About 50 to 100 mg of heparin solution are administered intravenously, undiluted, every 4 to 6 hours for one or two days, it is as a rule not necessary to give more than 250 to 300 mg a day The intervals between injections can be adjusted to this schedule The drug may also be administered in saline solution A 10 cc vial of heparin containing 10 mg is added to each 500 cc of saline and introduced intravenously, at the outset at a continuous infusion rate of about 2 cc (30 drops) a minute Again, the total daily dose seldom need exceed 300 mg Frequent observation and care are required to avoid variations in the rate of flow which can occur with variations in the position of the arm or when the apparatus is at fault For use deep in the subcutaneous tissues 200 to 400 mg in Pitkin menstruum as recommended by Loewe may be given every 48 hours, or a heparin product called Liquaemin (Roche) may be used subcutaneously The clotting time is checked frequently, it should be at 15 minutes and not over 25 Should hemorrhage occur heparin is promptly discontinued, if the hemorrhage is severe, whole blood should be administered without delay

Dicumarol is given by mouth, it acts more slowly the effect is more lasting and is easier to control than heparin After determining the prothrombin time beforehand 300 mg is given The prothrombin level of whole plasma is tested frequently once a day at least The normal prothrombin time is 12 to 14 seconds it should be kept, under dicumarol treatment at 25 to 30 seconds The drug is stopped at once if the prothrombin time is over 30 seconds or the drug is reduced and daily amounts kept to 50 to 100 mg if the prothrombin time is less than 25 seconds It should never be given unless the prothrombin time is known and carefully followed When large amounts of dicumarol are given over several days and then completely stopped, the prothrombin time may remain prolonged

some when they occur with cardiac arrhythmias or heart failure as in acute myocardial infarction Giddiness or lightness of the head however, are not always manifestations of circulatory disturbance other causes should therefore be excluded and smoking prohibited Barbiturate and morphine preparations may aggravate the symptoms Rigorous restriction of sodium in the diet sometimes alleviates them

Respiratory Difficulties The inhalation of oxygen sedation and respiratory stimulants are the measures indicated If morphine is employed depression of the respiratory centers must be avoided The drug is invaluable if pulmonary edema is threatening or established Keeping the throat and nasal passages clear and the use of a back rest help the breathing The treatment for respiratory disturbances due to cardiac failure consists largely of bringing aid to a failing circulation aminophyllin and digitalis sometimes caffeine parenterally administered are excellent Coramine as a respiratory stimulant given alone or combined with aminophyllin intravenously or intramuscularly is valuable the dose of coramine is 1 5 cc repeated every 1 or 2 hours as required An oral preparation of coramine is available the dose is 1 to 3 cc (M 15 to 45) every few hours The liberal use of aminophyllin by vein despite a certain degree of danger which attaches to this route of administration can bring striking benefit It should be given rather freely 10 cc containing 0 24 (gr 4) of the drug every eight hours or oftener and the interval increased as the patient improves Glytheonate has been recommended as a good oral preparation of aminophyllin It consists of theophyllin buffered with sodium glycinate 1 to 3 tablets are given every 4 to 6 hours Aminophyllin may also be given by rectal route the dry drug 0 5 to 0 75 is dissolved in about 150 cc of distilled water and introduced rectally every 6 to 8 hours Camphor in doses of 0 2 to 0 3 (gr 3 to 5) given in oil and subcutaneously is still employed but its value is overrated

Gastro-intestinal Manifestations These are frequently mild but if severe or unchecked may tip the scale between a good and a bad outcome Most of the complications are parasympathetic in nature

Flatulence During the acute stage of illness local applications stupes are to be avoided or carried out only with the greatest care the water must not be too hot the cloths not too heavy and the duration of the treatment short Enemas are dangerous instead a glycerin suppository is inserted in the rectum or a small amount of bland oil an ounce or two 30 to 60 cc instilled in the rectum through a small caliber catheter The use of a rectal tip to keep the sphincter open is of some use Carminatives must be chosen wisely a few drops of Hoffman s anodyne on a small lump of sugar dissolved in the mouth a small quantity of fairly warm freshly brewed tea or concoction of Chamomile tea or other herbs like peppermint etc may bring relief Small doses of charcoal 0.3 to 1 5 (gr 5 to 25) or the ready made Eucarbon tablets (containing a small amount of cascara) are good Sometimes small doses of calcium carbonate 0 6 to 2 0 (gr 10 to 30) or Kaolin 4 to 8 (gr 60 to 120) bring relief Soda

as a preventive of ventricular fibrillation which may be induced by reflex coronary constriction has not yet been proved

(6) *Acute Pulmonary Edema* The pulmonary, smaller, circulation (it includes as an "accessory auricle" the liver veins to their "exit barrier") is not only the first to receive the brunt of congestive failure but the last to be rid of its effects The rate of blood flow in the pulmonary venous vessels is retarded and does not return to normal until the pulmonary circulation is free of congestive failure The velocity of pulmonary venous blood flow, therefore may be looked upon as a barometer of the development and recession of pulmonary congestion and in turn of congestive heart failure The practical therapeutic point is that the treatment of congestive failure is not completed, regardless of all apparent amelioration, until the rate of blood flow in the pulmonary venous channels is restored to normal (Blumgart et al ,[6] Hitzig,[16] Miller,[5] Miller and Furman[27])

Sudden heart failure in the form of acute pulmonary edema can come early in the cardiac attack or days later This dread complication, a sequel frequently of sudden left ventricular failure, is the most dramatic form of heart failure and a sharp threat to life Factors other than increased obstruction to pulmonary blood flow are probably necessary to produce pulmonary edema anoxia *for example with its effect on pulmonary capillary permeability and* shifts in the amount of plasma protein (Cameron[7]), but whatever the mechanism, at the first sign of pulmonary congestion (or general edema) treatment should be prompt and energetic Oxygen therapy *should be started at once* Some patients are relieved promptly by a single dose of morphine 0 01 to 0 015 (gr $\frac{1}{6}$ to $\frac{1}{4}$) combined with atropine 0 0006 (gr $\frac{1}{100}$) even before time permits the use of oxygen The atropine in the same or lesser quantity may be repeated every 15 to 20 minutes for a few doses The weakening left ventricle sometimes needs the help of caffeine sodium benzoate 0 12 to 0 3 (gr 2 to 5) injected parenterally Ephedrine in oil 0 015 (gr $\frac{1}{4}$) combined or preceded by aqueous solution (gr $\frac{1}{8}$ to $\frac{1}{4}$) may be useful A good remedy is the intravenous introduction of strong hypertonic glucose solution 50 cc of 25 or 50 per cent to which aminophyllin may be added 0 26 or ouabain 0 025 mg or at most 0 5 mg at any one time The ouabain may be repeated in 0 1 to 0 2 mg units every few hours The total amount should not exceed 1 0 mg in twenty four hours and it is best not to use it at all if the patient is still under the effect of digitalis Venesection may be life saving Two hundred to 500 cc of blood are withdrawn, the effect of a small amount removed is striking and sudden enough to suggest a reflex mechanism

(7) *Congestive Heart Failure (General Anasarca)* This is discussed on p 290

Other Complicating Manifestations

Dizziness and Vertigo These symptoms may be mild or fleeting as in mild and brief attacks of acute coronary insufficiency or they may be severe and trouble-

venously by a slow drip method about 1 to 2 cc per minute This is repeated within twenty four hours Sodium chloride may be needed to replenish chlorides lost by vomiting Drugs to overcome nausea are usually not efficacious although cerium oxalate 1 0 to 2 0 (gr 15 to 30) small oral doses or cocaine 0 015 (gr ¼) or chloralose 0 2 to 0 6 (gr 3 to 10) are recommended

Fatigue and Exhaustion In some respects fatigue and exhaustion save the individual from physical movement This advantage is greatly overbalanced however by the danger of collapse from the symptoms The victim of a severe acute myocardial infarction suffers from weakness in the heart as well as general exhaustion The weakness in the heart is no illusory matter It may prove to be a manifestation of the general autonomic reaction or of course of heart muscle injury For asthenia no specific remedy is known and resort is made to general methods warmth of the body maintaining the general circulation careful nourishment and preserving the patient s reserve strength by avoiding stress strain and exertion Desoxycorticosterone may be tried 1 to 2 cc parenterally one or two times a day small doses of strychnine 0 001 (gr $\frac{1}{60}$) with or without caffeine citrate 0 06 to 0 12 (gr 1 to 2) or ephedrine 0 015 (gr ¼) by mouth help The ingestion of large amounts of sodium chloride may be tried if heart failure is no factor Citrate salts (gr 30) three or four times a day have been recommended to overcome a tendency to mild alkalosis and thus offset asthenia

Sweating Intractable drenching sweats may become extremely troublesome and add to the exhaustion As long as it lasts the sweating represents a portent of the serious state of the patient Measures to alleviate this symptom are not always effective Restriction of fluid and of sodium chloride intake is of little value and needlessly adds to the discomfort of the patient Something is accomplished by attention to the weight of coverings and by alcohol sponge baths Drugs are of variable value belladonna 0 3 to 1 cc (M 5 to 15) or atropine (gr $\frac{1}{75}$) should be beneficial but often fail Gynergen 0 5 to 1 cc subcutaneously is not of striking benefit agaracin 0 005 to 0 02 (gr $\frac{1}{12}$ to ⅓) is sometimes good Sodium amytal in large doses 0 2 (gr 3) every two or three hours for several consecutive doses has been recommended The drug is supposed to act on cerebral centers bringing relief without any soporific effect

Hyperglycemia associated with glycosuria is an occasional complication of acute myocardial infarction and requires no therapy It is probably a central effect and subsides in short order The hyperglycemia and especially the glycosuria of a diabetic who suffers a cardiac attack may need prompt and vigorous attention Insulin therapy in such patients carries with it the hazard of causing vagal coronary constriction or liberation of adrenalin with a deleterious influence on the coronary vessels

Insomnia This is a central disturbance and difficult to combat A dread of dying in sleep not a rare experience in these patients makes the insomnia still more difficult to overcome The patient may hide this dread and the wary physician should be on the lookout for it and reassure the patient firmly and

bicarbonate 4 (gr 60) and charged or effervescent fluids are uncertain in effect, occasionally adding to the flatulence Syntrogel or Gelusil tablets, one after each meal and before retiring are useful, also Resinat, 1 or 2 capsules The regulation of all fluids and food is important in overcoming flatulence A regimen of liquids if given in small quantities not too hot or too cold, and food that is semi solid, easily digestible, occasionally small portions of fairly solid food, for example, toast, a small baked potato, cooked cereal that is firm, a small portion of well cooked puree of peas may turn the trick Raw fruits and their expressed juices and raw vegetables are best avoided Flatulence in some cases is relieved by the use of a vasodilator, nitroglycerin or amyl nitrite, each ampule of the latter contains 0 2 to 0 4 (M 3 to 5) The use of posterior pituitary extract 0 5 to 1 cc (10 to 20 units) and prostigmin (1 to 2000 or 1 to 4000 solution) 0 5 to 1 cc as advocated is much too dangerous in this type of patient Atropine may prove to be a good remedy

Constipation Allowing the patient to go without a bowel movement for several days after his acute cardiac attack is often a wise procedure However, should abdominal distress develop to an appreciable degree the bowels may require attention The mildest measures are the safest, 3 to 4 ounces of warm, bland oil instilled into the rectum, supplemented if well borne by several tablespoonfuls by mouth Glycerin suppositories may help as a rule not Small weak soap sud enemas, 6 to 8 ounces, are worth a trial, given slowly Colon irrigations, as a rule, are contraindicated but when resorted to they are to be carried out with great care, a few ounces at a time allowed to go into the rectum and then promptly siphoned off The entire procedure is not to take more than ten minutes, perhaps less, and stopped at the least sign of pain in the chest

Purges and all strong cathartics are generally best avoided There are patients, however, who do well especially after the severe initial illness on small daily doses of mild purgatives, such as milk of magnesia 8 to 12 cc (ʒii to ʒiii), Carlsbad salts 4 cc (ʒi) in a glass of hot water sodium phosphate 4 to 8 cc (ʒi to ʒii) or 4 cc (ʒi) soda bicarbonate in a glass of hot or cold water, etc The solid cathartics in small amounts, are good cascara sagrada (gr 5) or the senna preparation, glysennid one tablet at night The aim is to have a mild movement with as little effort as possible and not more than once a day, every other day may be good enough

Nausea This may come with the onset of the attack It is well to remember that morphine and similar products produce nausea and other medications are not free of this disadvantage Many patients never have nausea, in others nausea persists, also retching and vomiting These symptoms in acute myocardial infarction are dangerous because they may cause extension of a coronary thrombosis or a fresh thrombosis When fluids and carbohydrates are not retained or absorbed through the stomach intravenous glucose is indicated Five hundred to 1000 cc of 5 per cent glucose in saline solution or 10 per cent distilled water (less likelihood of local venous thrombosis) are administered intra

standing of his physician and of other persons around him the confidence he has in his treatment all play their part to this end Yet if pain is severe and stubborn aside from the use of oxygen therapy which brings relief in the early days after an attack resort to drugs for the longer subsequent periods becomes the mainstay for easing pain and for bringing relaxation rest and sleep These drugs have already been described their selection and the frequency with which they are administered are determined by the need in each case The drugs to ease pain are more than anodynes and analgesics, they are invaluable calmatives The abolition of pain or its appreciable reduction or even increasing the interval between attacks are invaluable not only because of the relief but also because absence or mitigation of pain helps conserve the strength of the patient and thus further his recuperation The drugs carry with them certain drawbacks already discussed A general disadvantage that derives from the eradication of pain by any means is the disappearance of the warning signal function of anginal pain (Chapter II), but this disadvantage is no contraindication to striving for relief It is well however to re-emphasize that in the absence or abolition of pain the underlying malady and the menace that goes with it still exist

The patient sometimes procures grateful relief of pain from the use of simple measures such as the application of heat to the precordium or gentle counter irritation from a mustard plaster or rubbing with methyl salicylate Precordial pain also the radiation into the arm are eased and lessened on occasions by placing the left arm in a special position or posture by immobilizing the arm as much as possible or by exerting strong pressure upon the nerves of the arm implicated in the distribution of pain Libman procedure [9] This latter manipulation is not to be undertaken lightly when the patient although convalescing is still seriously ill Cold applications (ice bag) are not welcome occasionally however they relieve precordial pain notably when tachycardia is a feature

The pain of acute pericarditis is of a different order its reference is by way of the phrenic pathways to the trapezius muscle Sometimes a pericardial rub is audible and pain absent However when pain is present it is apt to be aggravated as the patient shifts from side to side and a fairly frequent complaint is the intensification of pericardial pain from resting on the left side For pericardial pain an ice bag may be helpful, sometimes heat occasionally strapping the chest when there is pleuropericardial involvement, and sedation

Dyspnea

This is almost always a feature of heart failure associated often with troublesome almost intractable cough and disturbed rest and sleep Mechanical pressure by an engorged left auricle on the left recurrent laryngeal nerve can aggravate the cough and add to the dyspnea The remedy is vigorous treatment of the heart failure with diuretics digitalis strophanthin aminophyllin etc Watching the weight increase is a reliable way of estimating fluid increase in

with good common sense, or explore the psychologic aspects of the fear It is not advisable to "push" morphine or allied drugs lest unpleasant and stubborn after effects and addiction appear Chloral hydrate by mouth may be valuable 0 3 to 0 6 (gr 5 to 10) it is also given per rectum, repeated in three to six hours in larger amounts in some cases Severe insomnia is sometimes broken by the milder sedatives The general management, quiet of the room, the elimination of disturbing factors are conducive to sleep

Part II Interval and Chronic States

Treatment

After the violence of the attack has subsided, the patient will be left spent, or if no serious cardiovascular lesion exists as in many cases of acute coronary insufficiency he may exhibit an immediate and almost miraculous recovery The attack of acute myocardial infarction can be brief, too, and the patient will pass through a short period of convalescence His subsequent course will be governed by the absence or recurrence of pain, mental anxiety, and his ability to function in accordance with the demands made upon him Therapy may call for little more than wise counsel and careful instruction to avoid situations which precipitate an attack Freedom from attacks and a sense of comparative well being, however, are no guarantee of immunity from the danger of succeeding attacks or sudden death The care from now on is largely preventive, and the predisposing and excitatory factors which bring on an attack must be shunned or guarded against

But in a great many patients with acute myocardial infarction the acute episode is followed by sickness and disability for weeks and even months and some individuals who develop recurrent infarction or progressive alteration of the coronary tree become permanent invalids

The patient with an acute myocardial infarction is kept in bed during the first three to four weeks of illness This period is best not shortened even if the attack seems to be mild The period of bed rest, with certain exceptions is wisely not prolonged because of the danger of pulmonary embolization especially from undetected venous thrombi in the lower limbs The extremities are carefully and frequently moved to minimize this danger When he is ambulant he is supervised for months under orders to avoid fatigue or strain During the immediate period of convalescence and for months thereafter, he may develop pain or fatigue, exhaustion, dyspnea psychic disturbances The gravest danger is heart failure, or acute pulmonary edema (Cameron[7]) In some cases therapy and management may have to be continued for the remaining life span of the patient

Pain

The alleviation of pain is not a matter of drugs altogether The general comfort of the patient, the skill with which he is nursed, the psychologic under

standing of his physician and of other persons around him the confidence he has in his treatment all play their part to this end Yet if pain is severe and stubborn aside from the use of oxygen therapy which brings relief in the early days after an attack resort to drugs for the longer subsequent periods becomes the mainstay for easing pain and for bringing relaxation, rest and sleep These drugs have already been described their selection and the frequency with which they are administered are determined by the need in each case The drugs to ease pain are more than anodynes and analgesics they are invaluable calmatives The abolition of pain or its appreciable reduction or even increasing the interval between attacks are invaluable not only because of the relief but also because absence or mitigation of pain helps conserve the strength of the patient and thus further his recuperation The drugs carry with them certain drawbacks already discussed A general disadvantage that derives from the eradication of pain by any means is the disappearance of the warning signal function of anginal pain (Chapter II) but this disadvantage is no contraindication to striving for relief It is well however to re-emphasize that in the absence or abolition of pain the underlying malady and the menace that goes with it still exist

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the body, and as little as one pound of edema fluid may bring on dyspnea, especially of the nocturnal type

Extracardiac causes of dyspnea demand attention to the specific trouble in each case Removing these causes can add greatly to the chances of recovery of heart failure

Psychic Disturbances

For the psychic disturbances that trail an attack of angina pectoris or acute myocardial infarction, it is good practice to vary the sedatives and hypnotics A fairly large number of individuals differ in their response to these drugs and in some cases fears, uneasiness, bad day or night dreams, depressive states or exhilarated and manic states are produced by some of these drugs The barbiturates are frequent offenders in this respect, morphine and its derivatives to a lesser degree The mental anxiety is removed sometimes by measures that relieve the physical symptoms by nitrites, atropine, papaverine or other antispasmodics which ameliorate or abolish constriction or oppressions of the throat, chest or epigastrium and in this way allay 'fears of choking '

As the hours and days of acute illness draw to a close the physician will have opportunities to sense and learn the background of the patient the capacities of discipline, of stoicism, and for hope *The patient must suffer no betrayal* of confidence even in matters that seem trivial The understanding and mutual confidence established in the very beginning of the illness will prove a foundation stone upon which to build a skillful psychological bridge between patient and physician for the future Members and close friends of the family also are to exercise caution and a cheerful demeanor in the presence of the patient and here too an instinct for family and personality values will guide the physician in his counsel

Congestive Heart Failure

When the infarcted heart muscle fails to heal or after healing remains weak, the patient may sooner or later develop myocardial insufficiency manifested chiefly by a reduced cardiac reserve with congestive failure absent or minimal or congestive heart failure may dominate the situation A number of procedures are available for treating congestive failure (a) rest in bed or modified ambulatory treatment, (b) restriction of sodium intake (c) the use of diuretics (d) digitalis especially when the rhythm is deranged and (e) mechanical measures to remove dropsical fluid

(a) *Bed rest* Confinement to bed alone seems to have a diuretic effect With bed rest alone four or five pounds of dropsy may go in as many days provided no excess of salt was ingested This procedure in the greatest number of cases however, is ineffective In addition to bed rest, at least in the early period following a cardiac attack, the patient may have to be treated by supplementary measures i e, marked restriction of sodium intake the administration of

mercurial diuretics to promote elimination of sodium and water and with digitalis

(b) *The rigorous reduction of sodium intake* and adherence to this regimen is extremely important and itself sufficient ofttimes to rid the patient of edema and keep him edema free The severe regimens limit the intake to 200 mg of sodium which is equivalent to 0 5 Gm NaCl, or the sodium in the diet may be doubled This is accomplished by substituting salt butter for sweet Too long on this restriction can cau e general weakness malaise and irritability and salt intake may have to be increased. Fluids are not strenuously curtailed as in former regimens 1000 cc of milk and about 1500 to 2000 cc of plain water are permitted Overenergetic or too rapid dehydration is avoided The patient is weighed frequently daily if possible

The following compiled from a number of sources, is a useful restricted sodium diet containing 200 mg Na equivalent to 0.5 Gm NaCl Nothing that is not mentioned on this list should be taken Drinking water which has been run th ough water softening equipment is not allowed U e no salt in cooking Take no soda bicarbonate

Meat or Fish 3 oz by raw weight of fresh beef lamb pork veal poultry or fresh fish oysters but no shellfish These foodstuffs must not be used in frozen form unless it is certain they have not been processed with salt smoked processed and canned products are selected with the same precaution They may be fried in unsalted vegetable fat (olive oil Spry Crisco Nyafat) or lard

Eggs one egg daily if egg is needed for dessert use one or two yolks not the white

Milk salt free milk Lanolac marketed by Mead Johnson Co is a salt free milk The directions come with the product The equivalent of a fluid quart may be taken daily

Bread low sodium bread 4 slices daily A good preparation is made by many bakeries. Passover bread (matzoth) the plain or the tea biscuit may be used

Cereals plain farina Wheatena rice rolled oats (oatmeal) puffed wheat puffed rice shredded wheat Pettijohn s macaroni spaghetti

Unsalted butter 4 squares (¼ inch thick) daily

Cheese made from salt free milk

Spices practically all except celery onion or garlic salt and no marketed sauce such as ketchup horse radish mustard etc

Vegetables 3 to 4 servings of the following the *frozen* products of those marked with an may be used

Asparagus	Cowpeas	Peppers
Bea s green	Cucumber	Potatoes white or sweet one daily
Beans lima green	Eggplant	Pumpkin
Beans na y dried	Endive	Radishes
Broccoli	Lettu e	Rutabagas
Brussels sprouts	Mushrooms	Soy beans fresh or dried
Cabbage	Okra	Squash
Carrots	Onions	Tomatoes
Cauliflow r	Parsley	Turnip leaves
Corn	Parsnips	Turnips white or yellow
	Peas	

Fruit all fresh raw or cooked fruits and fresh fruit juices all canned dried or frozen fruits if they contain no salt or sodium benzoate

Desserts: gelatin (not prepared gelatin desserts), honey, jam, jelly, marmalade, unsalted nuts

Beverages: Apple juice
- Chocolate (with salt free milk)
- Coca Cola
- Cocoa (with salt free milk; avoid "Dutch process" cocoa)
- Coffee

Ginger ale	Orange juice
Grape juice	Pineapple juice
Grapefruit juice	Postum
Lemonade	Prune juice
Lanolac milk, salt free	Tangerine juice
Orange crush	Tea

This diet alone may be sufficient to rid the patient of anasarca or it may be necessary to administer 1–2 cc. mercupurin daily or almost daily for several weeks and at longer spaced intervals during subsequent months. Kempner[1b] claims that strict adherence to the rice diet which he developed will remove even the massive edema of congestive heart failure and keep the patient edema free. He administers no digitalis, mercurials or other diuretics. The diet consists of cooked rice prepared from a daily allotment of 200–300 gm. of dry product supplemented by fruits, syrups, sugar. It contains 20 Gm. protein, 5 Gm. fat and not more than 150 mg. sodium and 200 mg. chloride. The total caloric value is 2000 calories. If 3000 calories are given, the protein is raised in ratio. Milk and condiments are interdicted. Patients who are kept on this diet for many months apparently develop no hypoproteinemia. The diet is rigorous and psychologically difficult to adhere to but it appears to have much merit in some cases. The more liberal diet outlined above may have to be resorted to and if need be supplemented by the administration of mercurials to keep water exchange in balance.

Fox and his associates[9] have suggested that giving sodium lactate followed by sodium and potassium acetates will remove anasarca associated under certain circumstances with decreased plasma sodium and acidosis. Their studies indicate that the restriction of sodium as employed at present may require modification in some cases at least. Salt substitutes have not been successful; they are seldom palatable.

(c) *Diuretics.* These make up several groups with individual differences and indications for use. The first group consists of urea; the second of acid and base forming drugs; the third, metal preparations especially of mercury; the fourth, purine drugs; the fifth, digitalis and allied drugs; the sixth, hormone products; the seventh, hypertonic glucose or sucrose solutions.

Urea is sometimes a good remedy; it is given in large amounts, 15 to 25 grams (ʒ 4 to 7) in solution three times a day (Miller and Feldman[96]). Despite its unpleasant and often objectionable taste some patients take it readily or school themselves to take it. The additional fluid intake needed to dissolve the

urea is more than balanced by the large quantities of urine passed Urea in these massive amounts may be given uninterruptedly for many months Some patients in our practice have taken more urea than the equivalent of their own body weight When edema disappears its reaccumulation is prevented by the continued use of urea even in smaller amounts Disadvantages to urea therapy are (a) it is not always effective (b) it produces itching and excessive thirst (c) it does not rid the body of enough sodium chloride and as we have already mentioned (d) it is hard to take Charged water as a diluent rids urea of much of its unpleasant taste

Acid and base forming drugs Of these ammonium chloride and ammonium nitrate are in most general use They are given in doses of 2 to 3 grams (gr 30 to 45) three times a day and are continued for weeks and months and as in the case of urea with no deleterious effect to the body and more particularly to the kidneys Of their own accord they may act well or their effect may be augmented by the simultaneous use of another diuretic like urea or again their chief role may consist in increasing the efficacy of administered mercurial diuretics Disadvantages are gastric upsets and in the case of nitrate salt methemoglobinuria

Base forming or alkali drugs have been proposed when acid drugs fail The dehydrating effect of potassium nitrate was known nearly a century ago Binger and Keith[5] confirmed the use of potassium salts They employed potassium chloride as suggested by Barker[4] with good diuresis and no injurious effect They also recommended potassium nitrate

The third group comprises metal preparations and of these mercupurin and mercuhydrin have the widest use * They are to the regulation of cardiac dropsy what insulin is to glycosuria Their intravenous administration is very effective The dose in the beginning may be 0 5 to 1 cc to avoid too sudden and drastic depletion After an interval of a few days 1 cc or more (not above 2 cc as a rule) are given Thrombosis in the veins injected and febrile reactions are rare Deaths have been reported from intravenous use and attributed to too rapid administration This does not seem to be the whole explanation The intramuscular route of administration is preferred by many who fear this effect or wish to avoid a possible thrombosing effect on the veins This is a very useful method the danger of local necrosis is not great The buttocks are good sites avoiding the sciatic nerves and alternating each buttock for successive doses

The mercurial preparations are also available in suppository form and worth using It may be very profitable to give a mercurial preparation almost daily or actually daily for several weeks or longer (Gold[12]) continuing four to five times per week to prevent reaccumulation of edema gradually increasing the interval

* Thiomerin a new mercurial preparation has recently been recommended It possesses excellent diuretic effect, has low toxicity and produces little local reaction The dose is 0 5 to 2 0 cc subcutaneously

Desserts gelatin (not prepared gelatin desserts) honey jam jelly marmalade unsalted nuts

Beverages Apple juice
Chocolate (with salt free milk)
Coca Cola
Cocoa (with salt free milk avoid Dutch process cocoa)
Coffee
Ginger ale
Grape juice
Grapefruit juice
Lemonade
Lanolac milk salt free
Orange crush
Orange juice
Pineapple juice
Postum
Prune juice
Tangerine juice
Tea

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in the patient with chronic congestive heart failure Diuretics that have been tried and found wanting at one time must not be permanently discarded

(d) *Digitalis* is one of the best remedies for ridding the body of cardiac edema especially where the dropsy has resulted from myocardial insufficiency in which auricular fibrillation plays a part Digitalis alone is almost a specific or digitalis is excellent in combination with one or several of the diuretics or the procedures already mentioned There is seldom need for great haste in its administration in chronic congestive heart failure

(e) *Mechanical measures* In cases in which diuretics were tried without success or lost their effectiveness after a time mechanical measures may prove valuable Every clinician of experience learns that in special instances the simultaneous removal of cardiac edema fluid from pleural or abdominal cavities or the lower limbs converts a hitherto ineffectual diuretic into a potent active agent Again mechanical removal of a large quantity of accumulated fluid is all that is needed to permit the body to carry out the brisk and adequate elimination of fluids unaided by other means The indications for thoracic or abdominal paracentesis or the withdrawal of edema fluid from the lower limbs by Southey tubes are seldom major problems The usual precautions of asepsis are imperative nowhere more so than in the use of the Southey tubes

The patient with congestive heart failure in whom dropsy is not to the fore but who suffers from myocardial insufficiency in other ways will need special care in preserving what cardiac reserve remains and adding to it Some cases need attention to liver disturbances (hepatic insufficiency) associated with some degree of jaundice It is claimed that the jaundice of myocardial insufficiency is not necessarily an expression of liver dysfunction Even if this be so the jaundice calls for special dietetic and other care Large amounts of multiple vitamins and crude liver introduced intramuscularly are recommended

Associated Metabolic and Endocrine Disorders

The incidence of coronary disease and angina pectoris in middle aged and somewhat older groups is of course, high and in these groups also many metabolic and extracardiovascular disorders are frequent Examples are obesity diabetes gout anemia especially the type associated with menopause and hypothyroid states Cardiovascular renal conditions and varied forms of generalized decrescent arteriosclerosis frequently coexist with angina pectoris and coronary artery disease This association of coronary cardiac disease and extracardiac disorders requires treatment of the noncardiac condition undertaken with due regard for the cardiac aspect of the case Treating the one often benefits the other The treatment however of the extracardiac associated condition for example diabetes mellitus or gout should not be too strenuous

Diabetes mellitus is associated not only with alterations in the coronary vessels but in many other parts of the vascular tree the victims are generally middle aged or older The diabetes offers no great problem in therapy as a rule but

until the drug is administered three, two or less times a week. Urea or acid forming drugs are sometimes employed as supplementary measures. In the presence or suspected existence of renal disease, mercurial as well as other metal containing preparations such as bismuth salts, are usually interdicted. To offset or prevent abrupt water depletion and an accompanying intoxication and exhaustion, effects which follow the excessive action of these mercurials, 2 to 5 grams of table salt by mouth after an initial large output of urine totalling 1000 to 1500 cc., may be given as recommended by Poll and Stern.[31]

The oral use of mercuhydrin is still a matter of investigation. The dose is 0.2 to 0.4 (gr. 3 to 6) three or four times daily, the urine should be watched for evidence of possible renal damage, and gastric disturbances avoided.

The fourth group of diuretics, purine drugs, has fallen into some disfavor because other drugs and methods have proved more dependable and effective. Pharmacologically these drugs are known to increase and improve the coronary circulation. However, all the pharmacological evidence is based upon animal experiments in situ or on heart lung preparations kept alive under painstaking but nevertheless artificial conditions. There is still no convincing proof that xanthine products have a similar effect on the coronary vessels in man. It must be stated with equal emphasis that neither can the contrary be proved and indeed, some clinical reports extol the effectiveness of these products. These drugs do not merit complete neglect, particularly such preparations as diuretin 0.3 to 0.6 (gr. 5 to 10) three times a day, theocalcin 8 to 10 tablets daily, euphylline 0.1 (gr. 1½) by mouth 3 to 4 times a day, theobromine 0.12 to 0.3 (gr. 2 to 5) three times a day, theocine 0.12 to 0.3 (gr. 2 to 5) three times a day and caffeine in concoction form or as citrate or the benzoate salt.

Some endocrine products possess a diuretic action: the pituitary extracts (0.5 to 1 cc.) in diabetes insipidus, thyroid substances 0.06 or more (gr. 1 or more) three times a day in nephrosis and parathormone (units 5 to 15) in cardiovascular renal edema. These products are sometimes given in intractable cardiac edema. Their use, however, is not routine.

Hypertonic solutions of glucose or sucrose, introduced intravenously are good diuretics. There is seldom any contraindication to their use but they are not always effective. The glucose solutions are administered in 25 or 50 per cent concentration, preferably in distilled water to lessen the likelihood for thrombosis and to avoid giving sodium; the preparations are buffered and injected rather rapidly. This may be repeated six to eight hours apart for several times. Glucose therapy is not always innocuous, we have the impression it has been followed by pulmonary congestion. Sucrose in 50 per cent solution is administered very slowly.

An interesting and strange variability in efficacy often characterizes the use of many diuretics. Drugs or other measures to produce diuresis tried and proved ineffectual, yet utilized at another time and under conditions that seem unchanged become vigorously active. This fact is not to be lost sight of in treat

compatible with a good degree of cardiac function and reserve (p ‹) constitute an ever present peril of sudden death This type of sudden death possesses several curious aspects In the first place it does not occur in all cases of pronounced coronary stenosis, this has been explained by the variable factor of the protective function of newly developed intercoronary and arteriovenous channels In the second place considering the extent and efficiency of such a collateral circulation able to keep the heart from faltering sudden death becomes difficult to reconcile with an abrupt mechanical exclusion of blood at the mouths of the coronaries since the increment of blood suddenly shut off must be negligible Thirdly this type of sudden death is not so common in other forms of ostial narrowing i e arteriosclerotic thickening

Most patients with cardiovascular syphilis suffer not only severe anginal pain but in later stages poor cardiac reserve and congestive heart failure antiluetic therapy for them must be undertaken with great caution if at all Since such individuals have a life expectancy that is short at most one or two years it might be asked is it ever sound to advocate this form of therapy attended as it is by risks? There are those who prohibit any form of antiluetic treatment fearing this form of therapy precipitates sudden death or congestive failure when luetic narrowing of coronary orifices is advanced A special contraindication attaches to the use of arsenical preparations especially when administered intravenously Arsphenamine for example is known to produce severe shock (Jarisch Herxheimer reaction) or acceleration and spread of the focal syphilitic lesion in the cardiovascular system (the therapeutic paradox of Wile[27 23]) These serious untoward results may prove fatal especially in the presence of congestive heart failure Congestive heart failure is treated by the measures already described (p 290) and anginal pain calls for the therapeutic procedures already discussed (p 274) The removal or alleviation of congestive heart failure is said to favor the return of temporarily suppressed anginal pain

Despite the arguments leveled at treating luetic heart disease sufferers with unrelieved torment even with recurring congestive heart failure have obtained relief by antiluetic measures The most recent methods depend upon penicillin although mercury arsenic and iodides are still employed Details of therapy are available in the literature

BIBLIOGRAPHY

ALLEN E V The clinical use of anticoagulants report of treatment with dicumarol in 1686 postoperative cases J A M A 1947 *134* 323

[1] —— The emergency treatment of vascular occlusions J A M A 1947 *135* 15

ALLEN E V HINES E A JR KVALE W F AND BARKER N W The use of dicumarol as an anticoagulant Ann Int Med 1947 *27* 371

BARKER M H Edema as influenced by low ratio sodium to potassium intake Clinical observations J A M A 1932 *98* 2193

[2] BINGER M W AND KEITH N M The effect of diuretics in different types of edema. J A M A 1933 *101* 2009

advanced decrescent changes as in the Kimmelstiel Wilson's syndrome are more difficult to treat If insulin is employed, anginal seizures from its use should be avoided Diabetics, especially in the older age groups, do quite well on fairly liberal dietary regimes and without insulin It is wise not to aim too rigorously at making the urine sugar free For the diabetic with coronary disease there is a special advantage *in adhering to a total calorie regimen below the standard* requirement for his weight, age, etc

Gout is by no means rare in individuals who suffer from coronary artery disease and myocardial damage A dietary factor perhaps underlies each respective condition or is possibly common to both The gout should not be treated too vigorously

Cardiac Cachexia A very unusual state of marked emaciation and asthenia, resembling in some respects Simmond's disease, *is sometimes encountered in* chronic advanced heart disease produced by myocardial damage This condition, termed "cardiac cachexia " is not understood although some of the features point to a neurohormonal disturbance The condition may resist treatment A course of insulin combined with a carefully selected high calorie diet, large amounts of vitamins, endocrine products (antuitrin S, etc) deserve a trial A point usually overlooked in this connection as in most patients with chronic heart failure, is the possibility of liver insufficiency associated with prolonged engorgement and stasis of the liver Large doses of multiple vitamins, intramuscular injection of 2 to 3 cc of crude liver every other day and amino acids orally and parenterally, etc , are worth trying

Cardiovascular Syphilis

Syphilis is not primarily a disease of heart muscle However, myocardial changes and spirochetes in the heart muscle have been found by Warthin[35] Cesa Bianchi[5] of Milan also reported a small group of cases with spirochetes and alteration of the heart muscle and later Norris[5] published similar findings in three cases The presence of spirochetes in heart tissue however is strongly disputed by Saphir[3] , at best it is rare

Lues primarily attacks the aorta especially the suprasigmoid portion Lesions confined to this part of the vessel are however not incompatible with a moderately long span of life and with fair comfort The condition is often undetected and even the Wassermann reaction is likely to be negative in about 50 per cent of the cases (Gallavardin and Gravier[13]) Except for the serum test all this is changed *when the pathological process creeps below* the level of the coronary orifices and into the sinuses of Valsalva, eventually deforming the aortic valve with incompetence of the valve as a mechanical sequence Two chains of events follow the incompetence of the aortic valve leads to enlargement of the left ventricle, later often to congestive heart failure and anginal pain develops as *the luetic process encroaches on the coronary* ostia actually obliterating their lumen The constricted ostia though frequently

[30] PAL, J Die Tonuskrankheiten des Herzens und der Gefässe ihre Biologie und Therapie Wien J Springer 1934

[31] POLL, D AND STERN J E Untoward effects of diuresis with special reference to mercurial diuretics Arch Int. Med 1936 *58* 1087

[32] SAPHIR O Syphilitic myocarditis Arch Path 1937 *13* 266 436

[33] SCHWARTZ S P Transient ventricular fibrillation A study of the electrocardiograms obtained from a patient with A V dissociation Recurrent syncopal attacks Arch Int Med 1937 *49* 287

[34] —— AND JEZER A Transient ventricular fibrillation The clinical and electrocardiographic manifestations of the syncopal seizures in a patient with A V dissociation Arch Int Med 1937 *50* 450

[35] WARTHIN A A Studies of the pulmonary artery syphilitic aneurysm of left upper division demonstration of Spirocheta pallida in wall of artery and aneurysmal sac Am J Syphilis 1917 *1* 693

[36] WEGRIA, R Personal communication (publication in press)

[37] WILE U J The treatment of syphilitic liver and heart a therapeutic paradox Am J M Sc. 1922 *164* 415

[38] —— Principles underlying the treatment of cardiovascular syphilis Am Heart J 1930 *6* 157

[39] WOODS R M AND BARNES A. R Factors influencing immediate mortality rate following acute coronary occlusion Proc Staff Meet Mayo Clin 1941 *16* 341

[40] WRIGHT I S MARPLE C D AND BECK D F Anticoagulant therapy of coronary thrombosis with myocardial infarction J A M A 1948 *138* 1074

—— —— AND —— Report of the committee for the evaluation of anticoagulants in the treatment of coronary thrombosis with myocardial infarction Am Heart J 1948 *36* 801

[6] BLUMGART H L, LEVINE S A AND BERLIN D D Congestive heart failure and angina pectoris The therapeutic effect on patients without clinical or pathological evidence of thyroid toxicity Arch Int Med 1933 *51* *866*

[7] CAMERON, G R Pulmonary edema Brit M J 1948 (May 22) 965

[8] CESA BIANCHI D Sulla miocardite sifilitica a tipo interstiziale La Clinica Medica Italiana 1914 *53* 542

[9] FOX C I JR McCUNE D J BLAKEMORE A H MOLOSHOK R E AND DELANGE S The disappearance of edema through diuresis following artificial elevation of plasma sodium and bicarbonate Bull N Y Acad Med 1948 *24* 394

[10] FRAENKEL A *Strophanthin Therapie Berlin J Springer 1933*

[11] GALLAVARDIN L Les angines de poitrine Paris Masson 1925

[12] —— La fibrillation ventriculaire J Med de Lyon 1927 *8* 453

[13] —— AND GRAVIER R Le diagnostic de l insuffisance aortique syphilitique et ses difficultés D après une statistique de 84 cas d insuffisance aortique solitaire de l adulte avec autopsie J Méd de Lyon 1931 *12* 539 567

[14] GERTLER M M AND YOHALEM S B The effect of atabrine on auricular fibrillation and supraventricular tachycardia in man J Mt Sinai Hospital 1947 *13* 323

[15] GOLD H The pharmacologic basis of cardiac therapy J A M A 1946 *132* 547

[16] HITZIG W M Measurement of circulation time from antecubital veins to pulmonary capillaries Proc Soc Exper *Biol* & *Med* *1934* *31* 935

[17] HOWARTH S McMICHAEL J AND SHARPEY SCHAEFER E P The circulatory action of theophylline ethylene diamine Clin Sc 1947 *6* 125

[17] KEMPNER W Some effects of the rice diet treatment of kidney disease and hypertension Bull New York Acad Med 1946 *22* 358

[17b] —— Treatment of cardiac failure with rice diet history of patient with myocardial aneurysm North Carolina M J 1947 *8* 128

[18] *KISCH B Strophanthin New York Brooklyn Medical Press 1944*

[19] LEROY G V AND SNIDER S S The sudden death of patients with few symptoms of heart disease J A M A 1941 *117* 2019

[20] LIBMAN F In discussion of A review of 18 months experience with total ablation of the thyroid for angina pectoris and congestive failure by BLUMGART H L BERLIN D D DAVIS D RISEMAN J E F AND WEINSTEIN A A J A M A 1935 *104* 17

[21] LINDNER E AND KATZ L N Papaverine hydrochloride and ventricular fibrillation Am *J Physiol 1941 133* 155

[22] LOEWE L Anticoagulant therapy with heparin Pitkin menstruum in thromboembolic disease Am J Med 1947 *3* 447

[23] McEACHERN C G SMITH F H AND MANNING G W The effects of intravenous injection of papaverine hydrochloride upon the mortality resulting from sudden occlusion of coronary arteries in dogs Am Heart J 1941 *21* 25

[24] MILLER H R The use of drugs in oil intravenously Tr Coll Phys of Philadelphia 1920

[25] —— The velocity of blood flow in part of the pulmonary *circulation Proc Soc Exper* Biol & Med 1934 *31* 942

[26] —— AND FELDMAN A Prolonged use of massive doses of urea in cardiac dropsy Arch Int Med 1932 *49* 964

[27] ——, AND FURMAN M Pulmonary blood velocity in congestive heart failure Velocity in pulmonary venous circuit Proc Soc Exper Biol & Med 1935 *32* 728

[28] NORRIS J C Myocardial Syphilis South M J 1933 *26* 399

—— Syphilis of the myocardium *and coronary arteries J A M A 1937 108* 169

[29] OPDYKE D F AND SELKURT E L A study of alleged intercoronary reflexes following coronary occlusion Am Heart J 1948 *36* 73

of the sympathetic dilators Katz and Jochim[33] claim the coronaries are constricted by sympathetics

While it is highly probable that the sympathetic (adrenergic) division dilates the coronary vessels it constricts nearly all other vascular territories including the vast cutaneous vascular bed It is commonly held that by way of exception the splanchnic vessels as in shock for example are dilated while the peripheral circulation is constricted But according to Tomb[114] in shock the splanchnic as well as the cutaneous vascular beds undergo constriction the skeletal vessels becoming dilated Much further study is needed to confirm these points However if it were an accepted fact that the coronaries are dilated by sympathetic nerves it would permit the interesting hypothesis that these vessels are endowed with a means of remaining open and filled during a generalized sympathetic hyperactivity characterized by wide spread vasoconstriction Wenckebach entertained such a belief It is however extremely likely that during such hyperactivity vagal coronary constrictors are brought into action and indeed become ascendant in their influence overcoming the effect of sympathetic dilatation Or it may be conceived that the activity of the coronary sympathetic dilators becomes excessive and eventually weak or paralyzed whereupon by default as it were vasoconstriction without or with vagal constriction takes place This latter mechanism is exemplified in the behavior of peripheral small blood vessels (p 80)

All these nervous influences on the coronary vessels and the heart are mediated through efferent pathways The vessels also possess an afferent supply of sympathetic and vagal fibers The sympathetic afferent fibers are the main pathways for transmitting pain from the heart into consciousness and to interrupt these pathways various surgical attacks have been developed These surgical methods do not attack pain or the conditions responsible for pain they merely intercept the pathways and so aim to prevent painful impulses from traveling along these routes

A number of fundamental and practical questions arise in connection with the surgical and allied procedures in respect to anginal pain (a) Do all or at least the bulk of cardiac and aortic afferent fibers converge upon one point or region or are there significant accessory afferent pathways? (b) Are all the cardiac afferent impulses carried to special zones in the spinal cord (or dorsal roots) i e to the left Th 1 to Th 4 levels only? (c) Can it be that anginal pain is conveyed into consciousnes without the intervention of nerve pathways? These questions bear upon a critical evaluation of the surgical attacks that have been proposed

(a) Do all or at least the bulk of cardio aortic afferent fibers converge upon one point or region? Nearly all these fibers converge in the upper portion of the thoracic sympathetic trunk and then pass over the left upper transverse loops (white rami communicantes) into corresponding posterior roots which in turn

CHAPTER XVII

Surgical Treatment

I Neurosurgery and Paravertebral Block

Anatomic and Physiologic Considerations

FROM the preceding chapters the reader will realize that anginal pain is an expression of autonomic disturbance, often with a predominant emphasis of the sympathetic system and that the pain is transmitted chiefly, if not wholly, by sympathetic fibers It is therefore not surprising that most surgical attempts at the cessation and prevention of cardiac pain have been directed to breaking these sympathetic routes

Basing their approach to the problem of heart pain on the contention of Ranson,[96] Ranson and Billingsley,[97] Holmes and Ranson,[41] Danielopolu,[17] and others who claim that the superior sympathetic cardiac nerve contains a large *group of efferent fibers exercising a constant tonic constrictive action on the* coronary vessels, Coffey and Brown[15] limited their operation to severing this nerve or removing its related ganglion, the superior cervical, and they reported good results Kerr[51, 65] also obtained relief and the prevention of further attacks of anginal pain from superior cervical ganglionectomy By ostensibly blocking the stream of efferent impulses to the coronary vessels these investigators believe they averted spasm of these vessels On the other hand, Richardson and White[99] as well as White[101] obtained poor results from this operation and abandoned the procedure

Clinicians speak of spasm of the coronary vessels in man but this is not an acceptable concept to all physiologists Indeed there is no unanimity of agreement *on the mechanism of the nervous regulation of these* vessels (p 94) Pharmacologic studies are often conflicting in the same species The coronary vessels of cold blooded forms the tortoise for example (Drury and Smith[22] Drury and Sumbal[23]), appear to possess an arrangement opposite to *that of* mammals, namely, vasodilatation is vagal and vasoconstriction sympathetic The investigations in mammals are contradictory but in the main point to vagal constriction and sympathetic dilatation Clinical observations favor the existence of sympathetic vasoconstrictor activity and an embryologic basis helps strengthen this point of view (Ranson[96]) The consensus however leans toward a vagal constrictor influence over the coronaries in man and to a vasodilator action by sympathetics Physiologists like Anrep and co workers[1-4] *Hochrein*,[39, 40] Rein,[98] Wiggers[107] while not oblivious to the importance of the sympathetic dilators, emphasize the significance of the vagal constrictors others, Greene[34-37] Hinrichsen and Ivy[38] stress the predominant tonic action

the entire task of afferent conduction The failure of these operations could thus be accounted for without invoking the existence of afferent fibers in the ventral spinal roots Clinical observations also support these criticisms For instance, visceral pain, tabetic or anginal is not abolished sometimes until the excision of posterior dorsal roots is wide and in some cases bilateral (Davis[19]) Not only only rhizotomy and chordotomy but all other surgical approaches to stopping anginal and other visceral pain take on a new implication when viewed against the knowledge that visceral organs possess a diffuse and multiple arrangement of afferent fibers reaching all or most of the thoracic dorsal roots

(c) The third and last question is without the practical connotation of the other two It is nevertheless in some ways a challenge to our comprehension of the physiology of anginal pain The question is is it possible that anginal and other visceral pain occurs without the intervention of nerve pathways? Chemical substances more especially hormonal agents may play a role and perhaps also processes that are analogous to those of electrical induction a commonplace in the realm of physics On the basis of the knowledge available today we would be tempted to hold that any pain conceived to exist outside the anatomic pathways of the nervous system in strong likelihood would be very diffuse and probably lack the sharpness and other special qualities that characterize focused or localized pain However this argument would have little force against any weight of future evidence that pain travels by means other than nerve fibers

1 Sympathectomy

François-Franck[37] realized that the cervical sympathetic nerves transmit painful impulses from the heart into the central nervous system and as early as 1899 he suggested that division of these nerves would stop anginal pain The suggestion lay dormant for 17 years No one had enough interest or courage to put it to the test until 1916 when Jonnesco[48-50] of Bucharest later with Gomoiu[51] brought complete relief to some anginal sufferers by removing cervical sympathetic ganglia and nerves rather widely on both sides Despite complications and fatalities (six of the nine cases were lost) the feasibility of a surgical attack on anginal pain was demonstrated From then on various types of cervical sympathectomy were elaborated These gave relief in some cases but unfavorable postoperative consequences and a high mortality rate were deterrents to a wider trial (Bruning[13] Danielopolu[17] Kappis[54] Kummel[56] Fleth[93] and Tuffier[115])

Coffey and Brown[15] urged that removing a smaller portion of the cervical sympathetic system and on one side would circumvent these untoward results This appealed to Cutler and Levine[16] Leriche and Fontaine[61-63] White[111-114] and others

Danielopolu[17] worked out an extensive technic of his own sparing the stellate ganglion but cutting all the afferent pathways from the cardio aortic region to the central nervous system He performed the operation in two stages At the

enter the dorsal grey matter of the cord. Theoretically, at least, this zone of convergence, i.e., upper white rami with their corresponding posterior roots, aptly called a "bottle neck" by White,[11] would seem to be the strategic locality of choice for the severance at one blow of nearly all cardio-aortic afferent fibers, and a number of methods for the surgical relief of anginal pain have, therefore, aimed at this region. Unfortunately, success has not always attended the attempts designed to break these pathways at this point. The failures, we believe, were due to the fact that the operations, no matter how well executed technically, left intact a number and variety of *accessory afferent pathways* and these (Chapter XI), although ordinarily of secondary significance, were able to carry the burden of afferent conduction. For this reason, in our opinion, even after fairly extensive surgical excision or obliteration of the upper white rami or contiguous nearby nerve structures, cardio-aortic pain in some patients persisted or underwent a change in quality or intensity or penetrated into new localities. When, however, important accessory afferent pathways were presumably absent or inadequate to transmit and register anginal pain, blocking this "bottle neck" area frequently was brilliantly successful.

(b) The unsuccessful results from surgical intervention raise another question related to the first one in some ways. Is the entry of all visceral afferent sensations of which anginal pain is an example always and predominantly limited to one small portion of the spinal cord, i.e., for the heart and aorta the left T 1 to T 4 levels? In the case of the heart and aorta, are there exceptional cases with a wider and more extensive series of entry fibers into the spinal cord? (The afferent impulses carried by the vagal system into the medulla and higher levels of the brain are not part of this discussion for the moment, nor those impulses again in the vagal system which may reach the superior cervical sympathetic ganglion.)

Important experimental studies on other viscera bear on this query. The investigations of Schrager and Ivy[10?] and of Davis and his collaborators[19-?] and particularly those of Ashkenaz[5] already quoted in Chapter XI, indicate that the gallbladder, for example, through its splanchnic innervation sends *afferent fibers into all or nearly all the thoracic posterior roots of the right side* and into a large number on the left side also. This signifies that nearly all (for practical purposes we may say all) the thoracic segments of the spinal cord are bilateral recipients of visceral afferent impulses. Consequently, the destruction of upper thoracic white rami or upper dorsal roots would still permit the entry of visceral afferent impulses into the spinal cord through intact lower thoracic dorsal roots and the reverse would also be true, namely, upper roots would function if the lower were destroyed. This chain of events Ashkenaz[5] duplicated experimentally and, with sound logic, he suggested that partial rhizotomy (Foerster,[30] Lehmann,[63] Wartenberg[116]) or chordotomy (Foerster and Gagel[31]), performed at a selective level of the cord, were open to the criticism that extra-spinal afferent fibers in the sympathetic trunk were left unharmed to take over

A method proposed by Raney[33] interrupts the communication to the neuraxis by surgery instead of alcohol block. He severed the rami communicantes 2-5 and the sympathetic trunk between levels Th 5 and 6 on the left side. Relief from pain was striking he claimed.

Coffey and Brown[15] obtained relief of anginal pain by excising just the superior cervical ganglion. Their book cites eight cases with death in two and mentions other investigators who reported on this comparatively simple procedure (Bacon,[4] Holmes,[43] Kerr,[51,53] Lambert,[89] Marvin,[8-50] Mortensen[54-55]). Since the superior cardiac nerve is not known to contain afferent fibers (Edgeworth,[22] Huber,[45] Ranson,[96] Ranson and Billingsley,[97] Holmes and Ranson,[44] Langley[49-51]) the relief obtained by removing the superior cervical ganglion or cutting its nerve was explained (Ranson and Billingsley, Langley, Holmes and Ranson, Danielopolu, Kerr) on the basis of severing efferent constrictor fibers to the coronary vessels thereby freeing the vessels from a constant constrictor influence (Coffey and Brown). But there is doubt of the existence of such constrictor fibers in the superior cardiac nerve and even if interrupted bilaterally other efferent fibers would still be left undisturbed in the middle, inferior and posterior sympathetic cardiac nerves.

Cutting the middle cardiac nerve alone is an unsatisfactory attack because the nerve is inconstant and when present contains a comparatively limited number of efferent or afferent fibers. Dividing the inferior cardiac nerve alone is also open to criticism (p. 68) since there is doubt of its coronary constrictor function. However, since the middle, inferior and posterior cardiac nerves contain afferent cardiosensory fibers, severing these afferent nerves is indicated if the goal is interruption of afferent pathways which convey pain to the neuraxis. Except in the case of the posterior cardiac nerves, the interruption is better carried out by cutting the white rami at Th 1 to 4.

2. Extirpation of the Stellate Ganglion

Leriche[64] believed that pain in the heart may be produced by reflex from the stellate ganglion and he brought relief by injecting a local anesthetic into the ganglion or extirpating it. But before him Jonnesco[48] advocated its removal as a means of suppressing painful impulses from the heart, coronary vessels and the aorta. Jonnesco's physiologic basis for ablation of the ganglion was open to objections. In the first place, although afferent fibers would no longer transmit pain from the coronary vessels, the vessels would still be subject to vagal constriction with resultant pain; in the second place the eradication of this ganglion needlessly mutilated a large number of important efferent nerves: accelerators to the heart, adjustors of sweating and pilomotor acts to the upper limbs and head region, regulators of the iris and the muscle of Muller. Danielopolu[1] protested against indiscriminate injury to these efferent nerves and he stressed the danger especially after bilateral stellate ganglionectomy of robbing the heart of its accelerator control and leaving it a prey to the unchecked hyper

first, which was sometimes alone sufficient to alleviate and prevent anginal pain, he severed the sympathetic trunk directly above the stellate ganglion. In addition, he cut the communicating rami from this ganglion to the sixth, seventh, eighth cervical and first thoracic nerves, taking care to divide these rami (on both sides if necessary) close to the spinal cord in order to avoid injuring a similar ramus that emerges from the first thoracic component of the stellate ganglion and connects with the second thoracic intercostal nerve; this lower ramus occasionally carries cardio accelerator fibers. He also divided the vertebral nerve.* *The following structures were then divided at this first stage*: the cervical trunk above the stellate ganglion, the connections between this ganglion and the lower cervical and first thoracic nerves, the descending cardiac branches from the superior and middle cervical sympathtetic ganglia and the cervical vagal branches, also the branches from the superior and inferior laryngeal nerves and those from the vagal trunk and the depressor nerve, when the latter exists or can be found.

After an interval of time, the second stage was performed if pain recurred or remained unrelieved. The upper cervical sympathetic trunk including the superior and middle cervical ganglia was removed thus severing the connections with the upper five cervical nerves and in addition the thoracic cardiac branches of the vagus were divided. Danielopolu[17] stressed the care necessary to avoid injury to the vagus trunk and to the superior and inferior laryngeal nerves; he recommended the two stage operation for the right side if pain persisted after left side intervention.

This two stage procedure has been included not necessarily because we recommend it or feel it possesses greater merit compared to others but rather because it constitutes a realization that *multiple* afferent pathways which connect the heart and aorta to the spine and brain must be interrupted. While the existence of afferent fibers has not been established in all the structures Danielopolu severs (the vertebral nerve for instance) final judgment on this point and others too should be deferred until complete electro physiologic investigations have been carried out on all the nerves in question.

Yates and Trewhella[19] culled the results of 44 authors who performed 138 neurectomies. Relief was complete in 44.5 per cent, partial in 27 per cent. The immediate mortality was low if cases of luetic aortitis were excluded.

* According to François Franck[89] the vertebral nerve contains sensory fibers. Langley,[90-91] however, a close student of the sympathetic system, maintained there was no appreciable number of sensory fibers in the vertebral nerve and, to quote his own words, he explained "the reflex movement which François Franck obtained on stimulating the end of the nerve passing to the lower cervical as due to his not having separated it from the small nerve from the seventh (or seventh or eighth) cervical running to the underlying longus colli muscle." Langley saw no object in severing this nerve in the hope that sensory fibers were cut. Except for Danielopolu and Cino Pieri,[92] whom the former quotes in his book, the vertebral nerve is hardly ever included in sympathectomy for cardiac pain.

41 per cent The element of great apprehension and fear marked before operation was allayed or abolished White and Bland[138] have advocated upper thoracic ganglionectomy for unilateral anginal pain if the patient is in only fair condition and has fair cardiac reserve But if his condition is better and the reserve fairly good they favor bilateral laminectomy with root resection

5 Section of the Posterior Spinal Roots (Rhizotomy)

The partial rhizotomy performed by Foerster[30] Lehmann[63] Wattenberg[116] and the allied procedure of chordotomy carried out by Foerster and Gagel[31] have already been alluded to also the objections raised to these procedures (p 307) The operation of rhizotomy section of the posterior spinal roots was claimed by Davis[19] to give complete relief from anginal pain for a long time He divided the first six thoracic posterior roots Although this type of surgery has the obvious advantage of being carried out under direct vision this is easily outweighed by the hazard attached to an extensive operation in subjects who have as a rule myocardial and coronary artery disease The objections to rhizotomy voiced by Ashkenaz (p 302) also are pertinent

The early impetus to neurosurgery in connection with anginal pain was responsible for procedures which led to poor results and even disaster These were soon modified or abandoned and two comparatively safe methods developed (1) cutting the depressor nerve and (2) alcohol block of the upper thoracic sympathetic ganglia

6 Cutting the Depressor Nerve

The depressor nerve is identified in lower mammals but not in man in whom its existence as a separate strand is disputed A number of earlier workers believed they succeeded in cutting this nerve in man and as proof they pointed to the clinical relief which followed the operation The general belief is that the nerve eludes recognition Severing the depressor nerve has been studied by Borchard[11] Danielopolu[17] Eppinger and Hofer[26, 27] Hofer[41, 42] Jonnesco[49, 50] Odermatt[80] Wenckebach[119]

7 Paravertebral Block

At the suggestion of von Bergmann Laewen[55] in 1922 performed paravertebral block for heart pain the outcome of this attempt is not known That same year Kappis[5] suggested the use of novocain injection in the neighborhood of the lower portion of the cervical spine to interrupt sympathetic and vagal fibers which convey cardiac pain Brunn and Mandl[14] utilizing novocain injection reported 6 cases in 1924

The following year Mandl[73-5] published his results in 16 additional cases and in his monograph of 1926[76] he reported on another group of 20 cases Of

activity of the vagus nerve, moreover, by obliterating important fibers with dilator action on the coronaries these vessels were deprived of their normal blood volume The danger of leaving the heart exposed to the uncontrolled influence of the vagus was voiced also by Spiegel[106] and by Braeucker[1] These fears however, are not always borne out by practical experience although irritation or injury to the stellate ganglion has led to disaster

Danielopolu[17] describes Leriche's experience of sudden and intense pulmonary edema immediately after injection of the stellate ganglion Laubry and Heim de Balsac[6] also recorded sudden acute pulmonary edema followed in a few minutes by death while injecting a local anesthetic solution into the stellate ganglion Pletnew[91] had two cases that developed immediate and intense cardiac collapse, after injecting alcohol into the stellate ganglion, and Pletnew cites Braeucker as having caused a similar untoward effect These very serious and highly dramatic reactions *Danielopolu attributes to a sudden failure of the* left ventricle brought on by a marked loss in the contractility of this chamber as a result of paralysis of cardiac sympathetic fibers This paralysis together with that of coronary vasodilators greatly reduced the blood flow to the myocardium with acute myocardial insufficiency and even death as consequences

The relief obtained by removing the stellate ganglion or for that matter the superior cervical ganglion seemed to strengthen the concept that the conduction of pain from the heart to the cord may take place independently of the somatic sensory system Spiegel[103–106] proposed that sensory somatic impulses may play a role in maintaining the excitability of the sensory visceral elements of the posterior horn of the cord After cutting the intercostal nerves and the brachial plexus, thus causing degeneration of the somatic sensory cells of the spinal ganglion, Spiegel and Hashimoto[107] produced pain by stimulating the cardio aortic pain fibers in the stellate ganglion

3 Interruption of the Posterior Cardiac Nerves

These nerves or rami run directly across the posterior mediastinum from the 2nd, 3rd and 4th sympathetic thoracic ganglia to the cardiac plexuses (Kuntz and Morehouse[57]) The fibers arise from these ganglia below the stellate ganglion and carry visceral afferent and efferent fibers The efferent fibers act as accessory accelerators to the heart while the afferent fibers serve as an accessory pathway for anginal pain (Fig 37) These fibers are not disturbed by removing the stellate ganglion by any neurosurgical procedure carried out cephalad to the first dorsal level Thus posterior cardiac nerves are able to convey pain to the neuraxis when the sympathetic cardiac branches have been severed

4 Upper Thoracic Paravertebral Ganglionectomy

Lindgren and Olivecrona resected the upper four thoracic ganglia including the stellate for severe cardiac pain They reported on 71 patients Complete relief was obtained in 44 per cent and severe symptoms were made milder in

81 per cent The element of great apprehension and fear marked before operation was allayed or abolished White and Bland[?] have advocated upper thoracic ganglionectomy for unilateral anginal pain if the patient is in only fair condition and has fair cardiac reserve But if his condition is better and the reserve fairly good they favor bilateral laminectomy with root resection

5 Section of the Posterior Spinal Roots (Rhizotomy)

The partial rhizotomy performed by Foerster[20] Lehmann[?] Wattenberg[?] and the allied procedure of chordotomy carried out by Foerster and Gagel[?] have already been alluded to also the objections raised to these procedures (p 302) The operation of rhizotomy section of the posterior spinal roots was claimed by Davis[?] to give complete relief from anginal pain for a long time He divided the first six thoracic posterior roots Although this type of surgery has the obvious advantage of being carried out under direct vision this is easily outweighed by the hazard attached to an extensive operation in subjects who have as a rule, myocardial and coronary artery disease The objections to rhizotomy voiced by Ashkenaz (p 302) also are pertinent

The early impetus to neurosurgery in connection with anginal pain was responsible for procedures which led to poor results and even disaster These were soon modified or abandoned and two comparatively safe methods developed (1) cutting the depressor nerve and (2) alcohol block of the upper thoracic sympathetic ganglia

6 Cutting the Depressor Nerve

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these 20 cases, 11 were permanently improved, 7 had a "satisfactory" result 2 were failures, and one died four days after the injection Mandl used novocain solution and injected the Th 1 to 4 levels on the left side His work placed the method on a firm basis

The procedure was modified by Swetlow[108] in 1926, he used strong alcohol solution to produce degeneration of the sympathetic fibers, introducing novocain beforehand as an anesthetic Five years after his first publication Swetlow[109–110] gave his results in 22 cases relief was obtained in 18 patients and no patient died after injection he injected as low as the 9th dorsal root in some instances The alcohol method of paravertebral block was soon taken up in this country and abroad

Reports in this country appeared from Richardson and White,[99] Mixter and White [illegible] Levy and Moore [70–] White[1 3] in 1936 stated that in about 70 per cent of his cases he had been able to procure permanent relief from anginal pain Failures in 30 per cent of the cases were attributed to errors in selecting suitable cases and to faulty technic * A group of 30 cases studied by Levy and reported by Marvin[79] showed considerable relief in 40 per cent, complete failure in 30 per cent and the rest unsuccessful Publications from abroad were in practical agreement (Woodbridge[1 3] duBose [1] Flothow,[9] Pletnew[94] Ruth[101] Berard[10] Leriche[64] Paraf and Dreyfus LeFoyer,[90] Jessen,[47] O'Shaugnessy[8 –88])

The later publications by White [1] Levy and Moore,[71] Perlow,[91] Mandl,[8] Grant[33] and White and Bland[1 6] provided a still larger basis for evaluating paravertebral alcohol block In the main the later results agreed with those obtained earlier White[1 4] and White and Smithwick[1 5] found that of 67 cases with intractable angina pectoris complete or nearly complete relief of pain was obtained in 52 per cent and severe attacks were reduced to a mild form in 35 per cent, the unsatisfactory results amounted to 9 5 per cent and 8 7 per cent died within two weeks of injection The latter authors stated "in our experience failure to relieve precordial pain and arm pain by this method has never been encountered in the presence of signs of an effective paralysis of the upper thoracic sympathetic fibers i e , vasodilatation and sudomotor paralysis of the upper extremities and Horner s sign " Horner s sign, according to them is not essential to success but paralysis of the nerves and sweat glands of the face and upper extremities is essential They were able to observe clear cut Horner s signs in less than one half of their available records The patients who retained a hot dry hand were permanently relieved of cardiac pain and attacks of pain invariably returned when the hand became moist within a few days

In a follow up of available cases Levy and Moore obtained permanent relief in 47 5 per cent and some relief in a total of 77 5 per cent and 22 5 per cent

* The persistence of accessory afferent fibers capable of taking over afferent conduction we believe is another explanation

of the cases had no improvement Anginal pain with radiation in a number of instances returned later into the identical territory and dermatomic zone temporarily relieved by the alcohol block Perlow[91] in 1942 reviewed a series of 22 advanced cases that had received no relief before paravertebral block was instituted one third of the group had constant pain He was able to get complete relief in 7 cases partial relief in 9 and no improvement in 6 cases

From 1927 on Mandl[77-79] employed novocain as well as alcohol for paravertebral block He published a group of 20 cases treated between 1940 and 1944 of which 16 received novocain and alcohol at the same time Ten of the 16 were strikingly improved and returned to work 2 died, and the others were slightly or questionably improved Mandl has continued to use novocain alone or novocain and alcohol in paravertebral block in a large number of cases and believes that the value of the procedure is established The results are good in about 65 to 75 per cent of his material[75]

White and Bland[126] found that of 75 patients treated by paravertebral block injection with alcohol 56 per cent were entirely or almost completely relieved of pain on the side of injection about 21 per cent showed fair results 8 per cent derived no adequate help and 8 per cent died as a direct result of the procedure

Pathological Effect of Alcohol

To throw light upon the puzzling recurrence of anginal pain in the same territory and dermatomic areas temporarily relieved by alcohol block Merrick[81] carefully investigated the degeneration and recovery of nerve fibers following alcohol injection into the sympathetic trunks and ganglia He used cats and injected the alcohol (95 per cent) into the ganglion or the ramus directly or by the established paravertebral approach Injection into a ganglion or close to it caused a permanent block of all the postganglionic fibers which originate from it the ganglionic cells were destroyed and after 35 days only a connective tissue scar remained Injecting alcohol into the ramus dissolved the myelin sheath of the nerves and the continuity of the axon was disrupted In about three month myelin regeneration could be noted a month later function was restored in the preganglionic fiber

He came to the conclusion that alcohol injection into the ramus may produce temporary block whereas complete surgical section produces permanent block * Since alcohol infiltration of the ganglion will destroy the cells of the postganglionic fibers a permanent and complete block of the nerves to the heart and the aorta may be accomplished by paravertebral injection but this is less likely to be the case when the rami are injected In the latter instance paralysis of the sympathetic nerves may prove to be transient

* According to White and Smithwick however cutting the rami may be followed by regeneration within a space of time resecting the ganglia is therefore preferred

Site of Injection

The site of injection is posteriorly and over the left upper four or five thoracic sympathetic ganglia Injection below this level offers no special technical difficulties, but the upper cervical ganglia are inaccessible For pain that is entirely or predominantly dextral the alcohol is introduced on the right side, and in bilateral radiations the treatment is bilateral

Two suggestions have been proposed as aids in selecting the levels for treatment (1) a careful preliminary survey of the epicritic and protopathic reactions of dermatomic skin zones to uncover the spinal cord levels that may be involved and (2) infiltration with local anesthetic solutions into selected thoracic sympathetic ganglia to distinguish the skin areas which receive referred pain from those which do not

Selection of Subject

The selection of suitable cases requires good clinical judgment and experience It has been stated that the most suitable cases are those of unrelieved and intractable anginal pain with little or no structural cardiovascular damage This would narrow the usefulness of this method The method, however has not been limited to such cases The anginal sufferer is more than likely to show cardiovascular alterations and sequelae which result from this damage Structural changes, therefore, have been no strong deterrent to instituting paravertebral alcohol block Neither heart muscle injury, unless recent and fresh, congestive heart failure, nor a very restricted cardiac reserve have been considered contraindications Indeed, it is in this type of case that relief of pain may be the greatest boon because surcease from pain may protect the patient from progressive exhaustion and so turn the tide Suffering intractable pain these patients will submit willingly to any proffered aid for they have little to lose but their unrelieved torment Rheumatic activity and syphilis are no contraindications

Complications

The postoperative complications of paravertebral alcohol block are as follows pneumothorax from inadvertent puncturing of the pleura or lung pleurisy or bronchopneumonia for the same reason and transient but sometimes prolonged and troublesome intercostal alcoholic neuritis lasting weeks and months From any of the proposed neurosurgical procedures as well as from alcohol block a number of untoward results and complications have been reported (a) Horner s syndrome, fully developed about 48–72 hours after operation (b) clinical signs and symptoms due to the interruption of sympathetic fibers to peripheral structures i e homolateral or bilateral suppression of sweating of the face, or the shoulder, neck, arm or pectoral region paresthesias flushing and hyperemia from loss of tone of blood vessels in any of these areas (this flushing

phenomenon may last two to three months) muscular weakness or atrophy of muscles in these regions increase in the skin temperature as much as 5 degrees F appearing four to eight hours postoperatively and lasting two to three weeks, (c) bradycardia (d) the persistence or the initial appearance of intense pain, homolateral as a rule and in any of the regions already mentioned (brachial

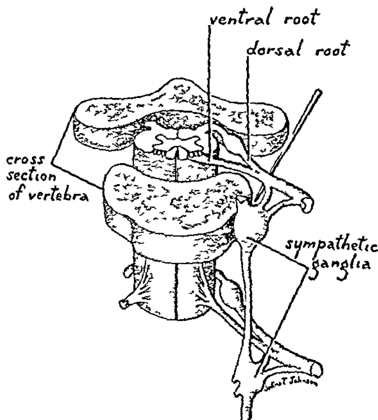


Fig 63 —The Relations of the Thoracic Sympathetic Ganglia to the Dorsal and Ventral Roots of Spinal Nerves at the Same Levels

neuralgia severe pain from chewing) and (e) syncopal sensations in the epigastrium or sensations of marked cardiac weakness

The neurologic consequences are not difficult to understand if one visualizes the anatomic relations of the sympathetic afferent fibers in the white and grey rami with respect to the sympathetic gangl onated chain and to the posterior and anterior (ventral) roots of the spinal nerves Figure 63 illustrates the relative positions of these structures within the retropleural space surrounded by loose connective tissue The sympathetic ganglia and their rami are situated

at least three quarters to one inch distant to the spinal roots and are separated from the latter by fibers of intercostal muscle as well as by retropleural connective tissue Furthermore, the posterior and anterior divisions of the spinal nerves lie within the intervertebral foramina, and as these roots emerge to form a common nerve trunk the nerve structures are still enveloped and protected by a prolongation of spinal cord covering The roots, therefore, may escape the effects of alcohol However, this is not certain Clinically, at least, paralysis of arm muscles innervated by the Th 1 and Th 2 components of the brachial plexus is not encountered Intercostal muscles do not seem to be paralyzed, but paralysis may elude ordinary clinical detection The instillation and diffusion of alcohol reaches the sympathetic ganglia and destroys (a) the preganglionic (myelinated) efferent fibers and the afferent fibers in the white rami and (b) the postganglionic (unmyelinated) efferent fibers in the grey rami

8 Other Methods

Two other methods have been recommended for the relief or abolition of referred anginal pain Both methods as we have remarked in Chapter III, have a common principle, namely, the reduction in the quantity of impulses in the somatic afferent neuron concerned with the reference of pain The total number of afferent molecular charges brought to the synaptic 'articulation' between somatic and visceral afferent neurones is reduced sufficiently to prevent the manifestations of radiation or reference of pain

The first method consists in anesthetizing the skin area of involved dermatomes (Weiss and Davis[117]) The second method originally recommended by *Danielopolu and Hristide in 1922 and 1923[18] and again reported by* Danielopolu[17] is aimed at the intercostal nerves, usually the left Th 1 to Th 4 These nerves are infiltrated with a local anesthetic or alcohol or severed completely The physiologic basis for these methods especially with regard to the second procedure has been attacked by Spiegel and Hashimoto [107]

The reflex of paroxysmal anginal pain has been treated by Rinzler and Travell[100] by local anesthetization of trigger zones in the pectoral muscles

When good success in relieving pain has been achieved, one need not lament the loss of pain as a danger signal The abolition of pain has advantages which outweigh the value of retaining pain as a warning or deterrent Moreover almost any one manifestation as much as any other of the upheaval that results from the mass action of the entire autonomic system, may carry the same weight as a danger or warning signal if properly evaluated

II The Artificial Vascularization of the Heart

The heart, rich in nutrient blood vessels is able in the course of years to call upon small unused channels *to help nourish the myocardium* altered by *obliterative* and other vascular changes as in the aging heart The adjustment between circulation and slowly advancing decrescent changes of heart muscle

is very gradual In the face however of a sudden disaster as for example the occurrence of a sudden occlusion of a large coronary trunk the heart cannot obtain urgently needed blood in amounts sufficient to meet the emergency in duced by the sudden deprivation of blood in the infarcted area The extra coronary system which exists cannot enlarge reflexly to transport enough blood to the injured muscle It requires months and years to grow collateral coronary channels

The extracoronary channels comprise two sets of tiny vessels One set em bedded in the fat at the base of the heart is made up of an extensive anastomo is of auricular blood vessels and coronary twigs with pericardio-phrenic branches of the internal mammary arteries and the anterior mediastinal pericardial bronchial uperior and inferior phrenic intercostal and esophageal branches of the aorta Despite its extent it can carry as already indicated little blood and hardly deserves to be designated as a vascular system Yet it may become expanded and enlarged enough to transport fairly good amounts of blood to the myocardium Accordin, to Hudson Moritz and Wearn [*] this may occur when the coronary system is extensively sclerosed

A econd group of extracoronary anastomoses can arise in adhesions which form between the surface of the heart and the pericardium (Moritz Hudson and Orgain[*]) The heart normally glides smoothly within and against its peri cardial envelope but after pericarditis numerous blood channels appear in the newly formed adhesions Thorel surmised that such cardio-pericardial vessels might act as an accessory blood supply for the heart

It occurred to Beck and his co workers to investigate whether these groups of inconsequential vessels could be vastly multiplied and expanded Animal ex perimentation convinced them[7-9] that these channels could be artificially de veloped into an extensive collateral vascular supply Var ous grafts were utilized fibrous pericardium pericardial fat omentum brought up through a diaphrag matic aperture or a pedicle of pectoral muscle the last held most promise Within about three weeks vessel in the graft grew into the coronary vessels These anastomoses could be augmented when the demands upon them were increased by various experimental methods i e shutting off coronary vessels etc In short by a variety of ingenious experimental devices it was demonstrated that an extracoronary supply of sufficient size and number to function as a real compensatory system was possible (Beck Tichy and Moritz[16]) Anastomoses in cardio-pericardial adhesions could be greatly increased by producing in flammatory reactions on the surface of the heart from irritation with foreign substances

The essential aim of these investigations is summarized by Beck Coronary occlusion is not a surgical stimulus but it can be effective in an indirect way Catastrophe can be averted by a small quantity of blood delivered where the blood supply is deficient By small quanti y is meant that which could be con sidered as a blood bath—enough to preserve viability of muscle so that it will

remain as muscle, and to prevent ventricular fibrillation If this crisis can be passed over so that the heart keeps on beating, then a good retrograde circulation can develop This small quantity of blood can be provided by surgical methods—by grafts and by inflammation on the surface of the heart The inflammatory agent that is best so far has been powdered asbestos This produces a reaction of inflammation and opens intercoronary communications"

Applying the principles and methods elaborated in animals to human beings with coronary sclerosis he proceeded to increase the extracoronary channels, ordinarily small and insignificant and lying in the fat at the base of the heart *and in cardiopericardial adhesions, and to establish a new and adequate arterial* or arteriolar supply for the heart The procedure was in some respects similar, as he himself pointed out, to the operation on the omentum for liver cirrhosis (Talma Morrison) except that arterial and not venous anastomoses were involved

The epicardium of the heart was removed to permit grafts to come into direct contact with the coronary vessels The pericardium was roughened to enable the pericardial fat receiving its blood supply from extracardial sources to grow onto the myocardium He used later powdered beef bone on the surface of the heart to induce a low grade inflammatory reaction between the heart surface and the grafts on the heart and for a graft he fashioned a pedicle from the left pectoralis major muscle The local use of procaine directly to the heart proved valuable, and drainage of the inflammation into the left pleural cavity was indispensable Patients were considered suitable for operation if the heart had suffered a diminution in blood supply from occlusive coronary disease and if protracted medical measures had been of no avail to diminish the disability or the severe symptoms Congestive heart failure was a contraindication

Feil and Beck [8] reported that of thirteen patients followed for five months or longer postoperatively three were free of pain, required no drugs and had acquired an increased effort tolerance, nine had less pain no increase in effort tolerance and needed medication from time to time, one patient exhibited some relief of pain and very slight increase in effort tolerance All thirteen had benefited to some degree at least *from the operation An interesting feature* was the marked emotional reaction with which operated subjects extolled the benefits of the operation Sixteen patients were living and nine dead eight succumbing one week after operation These statistics however should be appraised with the critical observation that while 50 per cent of the first twelve operated cases were fatal only 15 4 per cent of the subsequent thirteen cases died, and the last nine consecutive cases showed no mortality

More recently, Beck has attempted to revascularize the heart by converting the coronary sinus into an artery [9], dogs were used After ligating the coronary sinus he anastomosed into it a tributary of the aorta the carotid artery performing an end to end or side to side anastomosis He also employed in some instances, a graft of vein or artery as a connecting channel between the aorta

and the coronary sinus Arterialization of the coronary sinus made it possible to ligate a major coronary artery in the dog with little or no mortality and with little or no infarction Postoperative thrombosis did not intervene, as a rule

Beck carried out arterialization of the coronary sinus in a 45 year old man with angina pectoris who was almost totally incapacitated a segment of the left brachial artery was used for a graft Although the anastomosis was successful remaining patent even after death the patient succumbed after twenty four hours from a fresh myocardial infarction Beck has since tried the procedure on four other patients *

Although arterialization of the coronary sinus seems to be feasible in dogs several important questions have been raised these have a vital significance in connection with human subjects For example what are the incidence and dangers of postoperative thrombosis what is the optimal effective blood flow through the new channel and how can the flow be controlled is the venous drainage from the myocardium deleteriously disturbed what will be the eventual result of an arteriovenous fistula placed so close to the heart?

About the time when Beck made his first report on experimental revascularization of the heart O Shaughnessy et al [87–89] turned to the same problem developing vascular connections between the heart muscle and extracardiac vessels by the following measures (a) producing cardio-pericardial adhesion by the intrapericardial introduction of a sterile aleuronat paste (b) placing a *pedicled* omental graft in the pericardial sac and stimulating the production of adhesions between the omentum and heart with aleuronat (c) grafting omentum to the outer surface of the pericardium after producing cardio-pericardial adhesions In two cases at least collateral communications between the lung and the coronary circulation were established by grafting a lobe of lung to the myocardium The clinical improvement by these procedures was notable Of fifteen patients with angina pectoris ten lost their anginal symptoms and were able to return to profitable work Of five cardiac patients without angina one died as a result of operation and one of the remaining four became symptom free

Thompson[11] produced a successful collateral circulation in dogs by introducing sterile talc (hydrous magnesium silicate) into the pericardial sac With Raisbeck he recorded[113] the results on thirteen patients four died two showed moderate and seven marked improvement Thompson later[11] stated the results were good to excellent in more than 70 per cent of a group of 38 patients and in four the results were less than 33 per cent improvement and therefore classified as poor

BIBLIOGRAPHY

Anrep G V Regulation of coronary circulation Physiol Rev 1926 *6* 596
— Neue Untersuchungen über Physiologie und Pharmakologie der Kranzgefasse Arch exp Pharm 1928 *138* 119

* Personal communication

[3] ANREP G V AND SEGALL H N The central and reflex regulation of the heart rate J Physiol 1926 *61* 215

[4] ——, AND —— The regulation of the coronary circulation Heart 1926 *13* 239

[5] ASHKENAZ D M An experimental analysis of centripetal visceral pathways based upon the viscero panniculat reflex Am J Physiol 1937 *120* 587

[6] BACON J H Left superior cervical sympathectomy under local anesthesia in angina pectoris J A M A 1923 *81* 2112

[7] BECK C S The development of a new blood supply to the heart by operation Ann Surg 1935 *102* 801

[8] —— Further data on the establishment of a new blood supply to the heart by operation J Thor Surg *1936 5 604*

[9] —— The coronary operation Am Heart J 1941 *22* 539

[9] —— Revascularization of the heart Ann Surg 1948 *128* 854

[9b] BECK C S TICHY V I AND MORITZ A R The production of a collateral circulation to the heart Proc Soc Exp Biol & Med 1934–35 *32* 759

[10] BERARD M Les methodes du traitement de l angine de poitrine Lyon Rev 1937

[11] BORCHARD A Quoted by Kappis M *in* *Diskussions Bemerkungen Das Schmerz* problem der Eingeweide 46th Kongr Verhand d Dtschr Gesellsch F Chir 1922 Arch f Klin Chir 1922 *121* 188

—— Med Klin 1923 *19* 1696

—— Zur chirurgische Behandlung der Angina pectoris Arch f Klin Chir 1923 *127* 212

[12] BRAEUCKER W Der Brustteil des vegetativen Nervensystems und seine Klinisch chirurgische Bedeutung Beitr z Klin Tuberk 1927 *66* 1

[13] BRUNING F *Die operative behandlung der Angina pectoris durch Extirpation des Hals-* brust Sympathicus und Bemerkungen über die operative Behandlung der abnormen Blutdrucksteigerung Klin Wschr 1923 *2* 777

[14] BRUNN F AND MANDL F Die paravertebrale Injektion zur Bekampfung visceraler Schmerzen Wien Klin Wschr 1924 *37* 511

[15] COFFEY W B AND BROWN P K The surgical treatment of angina pectoris Arch Int Int Med 1923 *31* 200 1924 *34* 417

[16] CUTLER E C AND LEVINE S A Proc Inter State Post Grad Med Assembly of N Amer 1933 229

[17] DANIELOPOLU D L angine de poitrine et l angine abdominale Paris, Masson et Cie 1927

[18] —— AND HRISTIDE Recherches sur la sensibilité cardiaque Possibilité d améliorer l angine de poitrine par la résection des racines postérieurs ou des nerfs spinaux Compt rend Soc de biol 1923 *88* 201 Bull et mem Soc Med d Hôp de Paris 1923 *47* 69

[19] DAVIS L The surgical treatment of intractable pain J A M A 1933 *101* 1921

[20] —— HART J T AND CRAIN R D The pathways for visceral afferent impulses within the spinal cord Surg Gyn & Obst 1929 *48* 647

[21] —— POLLOCK L J AND STONE T T Visceral pain Surg Gyn & Obst 1932 *55* 418

[22] DRURY A N AND SMITH F M *Observations relating to the nerve supply of the coronary* artery of the tortoise Pt I Direct observations of the artery Heart 1924 *11* 71

[23] —— AND SUMBAL J J Observations relating to the nerve supply of the coronary arteries of the tortoise Heart 1924 *11* 267

[24] DU BOSE F G Therapeutic paravertebral alcohol block observations of its effect following its use in angina asthma and Raynaud s disease Am J Surg 1931 *11* 497

[25] EDGWORTH F H On a large fibred sensory supply of the thoracic and abdominal viscera J Physiol 1892 *13* 260

Eppinger H and Hofer G Die Therapie der Gegenwart Wien Klin Wschr 1923 *61* 169

—— and —— Zur Pathogenese und Therapie der Angina pectoris Wien Klin Wschr 1923 *36* 334

Feil, H and Beck C S Coronary sclerosis and angina pectoris J Thor Surg 1941 *10* 529

Flothow P G Diagnostic and therapeutic injections of sympathetic nerves Am J Surg 1931 *14* 591

Foerster O Die Leitungsbahnen des Schmerzgefühls u die chirurgische Behandlung der Schmerzzustande Berlin Urban u Schwarzenberg 192

—— and Gagel, O Die Vorderseitenstrangdurchschneidung beim Menschen Eine klinisch pathophysiologisch anatomische Studie Ztschr f d ges Neurol u Psychiat 1932 *138* 1

François Franck Signification physiologique de la resection du sympathetique dans la maladie, l epilepsie, l idiotie et le glaucoma Bull d l Acad Méd 1899 *41* 565

Grant F C In Stroud W D Cardiovascular Diseases Philadelphia Davis 1945

Greene C W An analysis of the efferent pathways and vasomotor control of the coronary circulation of the dog Am J Physiol 1931 *97* 526

—— The nerve control of the coronary vessels with new experimental evidence for the pathways of efferent constrictor and dilator neurones in the dog Am J Physiol 1935 *113* 361

—— Control of the coronary blood flow by reflexes arising in widely distributed regions of the body Am J Physiol 1935 *113* 399

—— An analysis of the relations of the coronary constrictor and dilator nerves in the cervical vagosympathetic of the dog Am Heart J 1936 *11* 592

Hinrichsen J and Ivy A C Effect of stimulation of visceral nerves on coronary blood flow in dogs Arch Int Med 1933 *51* 932

Hochrein M Der Koronarkreislauf Physiologie Pathologie Therapie Berlin J Springer 1932

—— Der Myokardinfarkt Erkennung Behandlung und Verhutung Dresden u Leipzig Th Steinkopff Ed 2 1941

Hofer G Bericht u die Durschneidung des Nervus Depressor bei dem Angina pectoris (nach Eppinger H u Hofer G) Ztschr f Hals u Ohren 1923 *6* 68

—— Surgical treatment of angina pectoris Wien Klin Wschr (supp) 1924 *37* 1

Holmes W Quoted by Coffey W B and Brown P K in Arch Int Med 1924 *34* 417

—— and Ranson S W Cervical sympathectomy in angina pectoris J Lab & Clin Med 1924 *10* 183

Huber K Über den Einfluss der Kranzarterienerkrankung auf das Herz und die chronische Myocarditis Virchows Arch 1882 *89* 236

Hudson C L Moritz A R and Wearn J T The extracardiac anastomoses of the coronary arteries J Exp Med 1932 *56* 919

Jessen H Die Neurologie und Neurochirurgie der Angina pectoris München med Wchschr 1938 *85* 1149

Jonnesco Th Traitement chirurgical de l angine de poitrine par la résection du sympathique cervico-thoracique Presse Médicale 1921 *29* 193 1923 *31* 517

—— Angine de poitrine guérie par la résection du sympathique cervicothoracique Bull de l Acad Med Paris 1920 *84* 93

—— Le sympathique cervico-thoracique Paris Masson et Cie 1923

—— and Gomoiu quoted by Danielopolu D in L angine de poitrine et l angine abdominale Paris Masson et Cie 1927

52 Kappis M Die operative Behandlung der Angina pectoris Med Klin 1923 *19* 1658

53 Katz L N and Jochim K Observations on the innervation of the coronary vessels of the dog Am J Physiol 1939 *126* 395

54 Kerr, H H Surgical treatment of angina pectoris Ann Clin Med 1925, *4* 30

54 —— Operative treatment of angina pectoris Ann Surg 1925 *82* 354

55 —— Personal communication to White J C Chapt 14, Diseases of the coronary arteries and cardiac pain edited by Levy R L New York, Macmillan 1936

56 Kummell H J Beobachtung und Erfahrungen an 52 Sympathectomien Zentralbl f Chir 1923, *50* 1434

57 Kuntz A and Morehouse A Thoracic sympathetic cardiac nerves in man their relation to cervical sympathetic ganglionectomy Arch Surg 1930 *20* 607

58 Laewen, A Über segmentare Schmerzaufhebung durch paravertebrale Novokaininjektionen zur Differentialdiagnose intraabdominaler Erkrankungen *Münch med Wschr* 1922 *69* 1423

59 Lambert, A Quoted by Coffey W B and Brown P K in Arch Int Med 1924 *34* 417 *Angina pectoris cardiac pain Am Heart J 1926 2* 18

60 Langley, J N The Autonomic Nervous System Cambridge W Heffer & Son 1921

61 —— The sensory nerve fibres of the heart and aorta in relation to surgical operations for the relief of angina pectoris *Lancet 1924 2* 955

62 Laubry C and Heim de Balsac R Considérations sur un cas de l angine de poitrine mortel Bull et mem Soc méd d Hôp d Paris 1934 *50* 1248

63 Lehmann W Über die sensiblen Fasern in der vorderen Wurzeln und ihre *Beziehung zur* Sensibilität der visceralen Organe Zschr f d ges exp Med 1921 *12* 331

64 Leriche R The Surgery of Pain Translated and edited by A Young Baltimore Williams & Wilkins *1939*

65 —— and Fontaine R Quatre observations d angine de poitrine traitées chirurgicalement Arch des maladies du coeur 1927 *20* 513

66 —— Surgical treatment of angina pectoris what it is and what it should be Am *Heart J* 1928 *3* 649

67 —— Deux nouveaux cas d angine de poitrine traitées chirurgicalement Arch des maladies du coeur 1929 *22* 588

68 —— Contribution à l étude de l angine de poitrine d origine traumatique Arch des maladies du coeur 1930 *23* 689

69 —— Chirurgie des nerfs du coeur J de chir 1932 *40* 508

70 Levy R L and Moore P I Paravertebral injections of alcohol for the relief of cardiac pain A review of experience to date and a report of nine cases Arch Int Med 1931 *48* 146

71 —— and —— Paravertebral sympathetic block with alcohol for the relief of cardiac pain report of 45 cases J A M A 1941 *116* 2563

72 Lindgren I and Olivecrona H Surgical treatment of angina pectoris *J Neurosurg* 1947 *4* 19

73 Mandl F Weitere Erfahrungen mit der paravertebralen Injektion bei der Angina pectoris Wien Klin Wschr 1925 *38* 759

74 —— Die paravertebrale Injektion zur Bekämpfung visceraler Schmerzen Wien Klin Wschr 1924 No 21

75 —— Die Wirkung der paravertebralen Injektion bei Angina pectoris *Arch f Klin Chir* 1925 *115* 136 1925 *136* 495

76 —— Die paravertebrale Injektion Vienna Springer *1926*

77 —— Die Funktionserkrankungen der Epithelkorper Die *Epithelkorperkrankheit* (Epithel korpersyndrom) Wien Klin W chr 1938 *51* 67 106

78 —— Paravertebral block in diagnosis prognosis and therapy New York Grune & Stratton 1947

Marvin H M An evaluation of the surgical treatment of angina pectoris Bull New York Acad Med 1935 *11* 4 3
—— Diagnosis of coronary artery disease New England J Med 194? *2?6* 251
Merrick R L Degeneration and recovery of autonomic neurons following alcoholic block Ann Surg 1941 *113* 298
Mixter W J and White, J C Pain pathways in the sympathetic nervous system Clinical evidence Arch Neurol. & Psychiat. 1931 *25* 986
Moritz A R Hudson C L and Orgain E S Augmentation of the extracardiac anastomoses of the coronary arteries through precordial adhesions J Exp Med 193? *58* 9?7
Mortensen M A Angina pectoris and its management Southwestern Med J 1924 *8* 10
—— Personal communication to Coffey W B and Brown P K Arch Int Med 1924 *34* 417
Odermatt W Die chirurische Behandlung der Angina pectoris. Dtsch Zschr f Chir 1923 *18?* 341
O Shaughnessy L An experimental method of providing a collateral circulation to the heart Brit J Surg 1936 23 665
—— Surgical treatment of cardiac ischemia Report of 6 cases of cardio-omentopexy Lancet 1937 23? 185
—— Slome D and Watson F Surgical revascularization of the heart The experimental basis Lancet 1939 1 617
Parat J and Dreyfus LeFoyer P Anesthésie du ganglion stellaire par voie paravertébrale Bull et mém Soc méd d hôp de Paris 193 53 116.
Perlow S Para ertebral alcohol injection for relief of cardiac pain Illinois M J 1942 *81* 55
Pieri G Pésultats éloignés d une intervention chirurgicale pour angine de poitrine (Méthode de la suppression du réflexe presseur) Bull et mém Soc méd l hôp d Bucarest 1928 *10* 211
Pleth V Cervical sympathectomy as a means of stopping pain of angina pectoris Am J Surg 19?? *35* *300*
Pletner D D Zur Fra e der Dauerresultate nach Anwendung der paravertebralen Alkoholinjektion bei An ina pect ris Ztschr f Kreislauf 1931 *23* 1?7
Raney R B A hitherto undescribed surgical procedure relieving attacks of angina pectoris J A M A 1939 *113* 1619
Ranson S W The cardiac nerves in angina pectoris Am Heart J 1925–26 *1* 508
—— and Billingsley P R The superior cervical sympathetic ganglion and the cervical portion of the sympathetic trunk J Comp Neurol 1918 *?9* 313
Rein H Die Phys ologie der Herz Kranzgefässe Ztschr Biol 1931 32 9 101
Richardson E P and White P D Sympathectomy in the treatment of angina pectoris Comparison with those from para ertebral alcohol injection Am J M Sc 1929 *177* 161
Rinzler S H and Travell, J Therapy directed at the somatic component of cardiac pain Am Heart J 1949 35 248
Ruth H S Diagnosti Prognostic and Therapeutic Nerve Blocks J A M A 1933 *10* 419
Schrager L V and Ivy A C Symptoms produced by distention of the gall bladder and biliary ducts A clinical and experimental study Surg Gynec & Obst *1928* *47* 1
Spiegel E A Ube das Wesen des Bauchschmerzes und seine Begleiterscheinungen Wien med Wchnschr 19?? 77 3 9
—— Wie Kommt es zur Generalisierung der Rindenerregung im Epileptischen Anfall? Wien Kli n. Wschr 1?2 4? 1159

[52] KAPPIS, M Die operative Behandlung der Angina pectoris Med Klin 1923, *19* 1658
[53] KATZ, L N, AND JOCHIM K Observations on the innervation of the coronary vessels of the dog Am J Physiol 1939 *126* 395
[54] KERR, H H Surgical treatment of angina pectoris Ann Clin Med 1925 *4* 30
[55] —— Operative treatment of angina pectoris Ann Surg 1925 *82* 351
[56] —— Personal communication to White J C, Chapt 14, Diseases of the coronary arteries and cardiac pain edited by Levy, R L, New York Macmillan 1936
[56] KUMMELL H J Beobachtung und Erfahrungen an 52 Sympathectomien Zentralbl f Chir 1923, *50* 1434
[57] KUNTZ A AND MOREHOUSE A Thoracic sympathetic cardiac nerves in man their relation to cervical sympathetic ganglionectomy Arch Surg 1930 *20* 607
[58] LAEWEN A Über segmentare Schmerzaufhebung durch paravertebrale Novokaininjektionen zur Differentialdiagnose intraabdominaler Erkrankungen Münch med W chr 1922 *69* 1423
[59] LAMBERT A Quoted by Coffey W B and Brown P K in Arch Int Med 1924 *34* 417 Angina pectoris cardiac pain Am Heart J 1926 *2* 18
[60] LANGLEY J N The Autonomic Nervous System Cambridge W Heffer & Son, 1921
[61] —— The sensory nerve fibres of the heart and aorta in relation to surgical operations for the relief of angina pectoris Lancet 1924 *2* 955
[62] LAUBRY C, AND HEIM DE BALSAC R Considérations sur un cas de l angine de poitrine mortel Bull et mem Soc méd d Hôp d Paris 1934 *50* 1248
[63] LEHMANN W Über die sensiblen Fasern in der vorderen Wurzeln und ihre Beziehung zur Sensibilität der visceralen Organe Zschr f d ges exp Med 1921 *1?* 331
[64] LERICHE R The Surgery of Pain Translated and edited by A Young Baltimore Williams & Wilkins 1939
[65] —— AND FONTAINE R Quatre observations d angine de poitrine traitées chirurgicalement Arch des maladies du coeur 1927 *20* 513
[66] —— Surgical treatment of angina pectoris what it is and what it should be Am Heart J *1928 3 649*
[67] —— Deux nouveaux cas d angine de poitrine traitées chirurgicalement Arch des maladies du coeur 1929 *22* 588
[68] —— Contribution a l étude de l angine de poitrine d origine traumatique Arch des maladies du coeur 1930 *23* 689
[69] —— Chirurgie des nerfs du coeur J de chir 193? *40* 508
[70] LEVY P L AND MOORE R L Paravertebral injections of alcohol for the relief of cardiac pain A review of experience to date and a report of nine cases Arch Int Med 1931 *48* 146
[71] —— AND —— Paravertebral sympathetic block with alcohol for the relief of cardiac pain report of 45 cases J A M A 1941 *116* 2563
[72] LINDGREN I AND OLIVECRONA H Surgical treatment of angina pectoris J Neurosurg 1947 *4* 19
[73] MANDL F Weitere Erfahrungen mit der paravertebralen Injektion bei der Angina pectoris Wien Klin Wschr *1925 38* 759
[74] —— Die paravertebrale Injektion zur Bekampfung visceraler Schmerzen Wien Klin Wschr 1924 No 21
[75] —— Die Wirkung der paravertebralen Injektion bei Angina pectoris Arch f Klin Chir 1925 *115* 136 1925 *136* 495
[76] —— Die paravertebrale Injektion Vienna Springer 1926
[77] —— Die Funktionserkrankungen der Epithelkorper Die Epithelkorperkrankheit (Epithel korpersyndrom) *Wien Klin Wschr 1938 51 67* 106
[78] —— Paravertebral block in diagnosis prognosis and therapy New York Grune & Stratton 1947

Author Index

105 SPIEGEL, E A Experimentelle Neurologie Berlin S Karger 1928
106 —— The mechanism of pain Internat Clin 1938 3 141
107 —— AND HASHIMOTO S Über die Schmerzleitung aus dem cardioaortalen System in Beziehung zu den Spinalganglion und den Ruckenmarksbahnen Zschr f d ges exp Med 1930 71 408
108 SWETLOW G I Paravertebral alcohol block in cardiac pain Am Heart J 1925–26 1 393
109 —— Alcoholic injections into nerve tissues for relief of pain Am J M Sc 1926 171 397
110 —— A clinicophysiologic study of the pathway of pain impulses in cardiac disease Am J Med Sci 1929 178 345
111 —— Angina pectoris paravertebral alcohol block for relief of pain Am J Surg 1930 9 88
112 THOMPSON S A An operation for the relief of coronary artery disease A preliminary report Quart Bull Sea View Hosp 1940 5 175
112 —— Personal communication
113 —— AND KAISBECK M J Cardio pericardiopexy The surgical treatment of coronary artery disease by the establishment of adhesive pericarditis Ann Int Med 1947
114 TOMB J W Shock and allied conditions Lancet 1937 233 1416
115 TUFFIER M Discussion de la communication de Jonnesco Bull d l Acad d Méd Paris 1921 86 70
116 WARTENBERG R Klinische Studien zur Frage der Geltung des Bell Magendieschen Gesetzes Ztschr f d ges Neurol u Psychiat 1928 113 518
117 WEISS S AND DAVIS D The significance of the afferent impulses from the skin in the mechanism of visceral pain Skin infiltration as a useful therapeutic measure Am J M Sc 1928 176 517
118 WENCKEBACH K Verh d Kongr f inn Med Wien 1923 35 1
119 —— Angina pectoris and the possibilities of its surgical relief Brit M J 1924 1 809
120 —— Klinik und Wesen der Angina pectoris Wien med Wchnschr 1924 74 671 736 907
121 WHITE J C Experimental and Clinical Studies in surgical treatment of angina pectoris Ann Int Med 1933 7 229
122 —— The Autonomic Nervous System New York Macmillan 1935
123 —— Chapt 15 Diseases of the Coronary Arteries and Cardiac Pain edited by LEVY R L New York Macmillan 1936
124 —— Technique and paravertebral alcohol injection methods and safeguards in its use in the treatment of angina pectoris 1940 71 334
125 —— AND SMITHWICK R I The Autonomic Nervous System New York Macmillan 1941
126 —— AND BLAND F F The surgical relief of severe angina pectoris methods employed and end results in eighty three patients Medicine 1948 27 1
127 WIGGERS C J Chapt 2 Diseases of the Coronary Arteries and Cardiac Pain edited by LEVY R L New York Macmillan 1936
128 WOODBRIDGE P D Therapeutic nerve block with procaine and alcohol Am J Surg 1930 9 278
129 YATER W M AND TREWHELLA A P The case for and against the operative treatment of angina pectoris Am J M Sc 1931 182 35

Subject Index